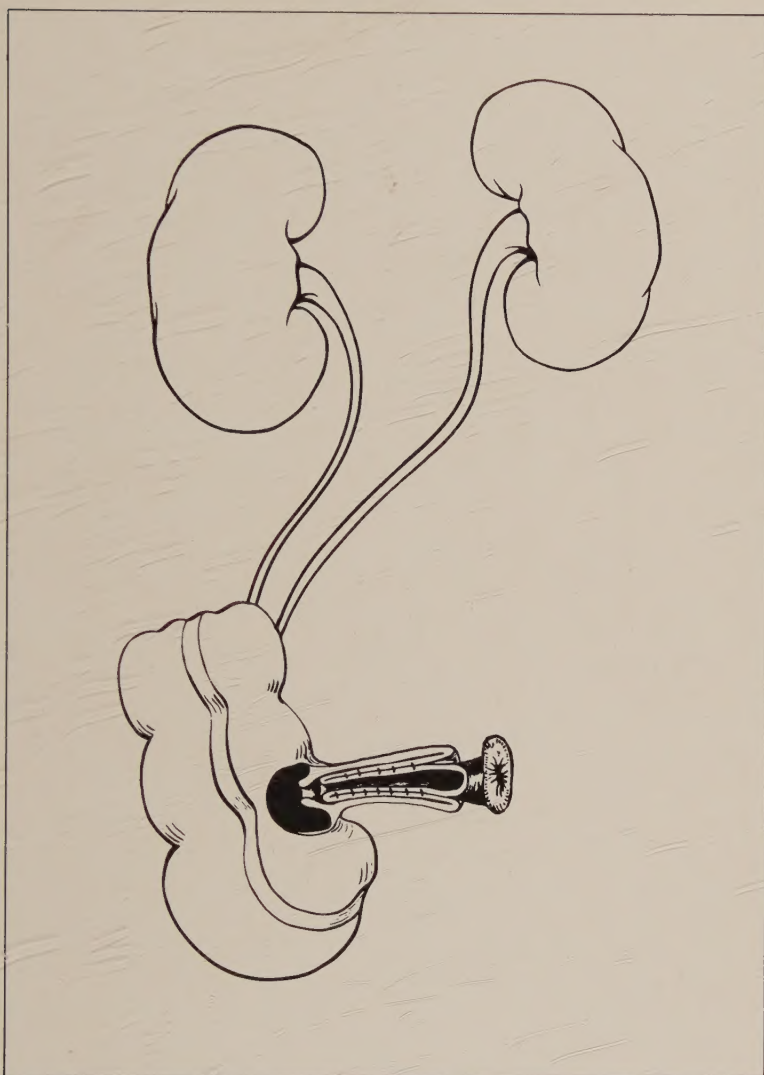




The Continent Caecal Reservoir for Urine

by
Wiking Månsson

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1984

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Lund, Sweden

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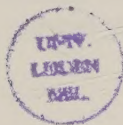
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The dissertation is based on the following papers:

- I** Månsson, W., Colleen, S. & Sundin, T.:
Continent caecal reservoir in urinary diversion.
Brit J Urol (in press).
- II** Hedlund, H., Lindström, K. & Månsson, W.:
Dynamics of a continent caecal reservoir for urinary diversion.
Brit J Urol (in press).
- III** Månsson, W., Mattiasson, A. & White, T.:
Acute effects of full urinary bladder and full caecal urinary reservoir on regional renal function. A study with scintillation camera renography.
Scand J Urol Nephrol (in press).
- IV** Månsson, W., Colleen, S., Forsberg, L., Larsson, I., Sundin, T. & White, T.:
Renal function after urinary diversion. A study of continent caecal reservoir, ileal conduit and colonic conduit.
Scand J Urol Nephrol (in press).
- V** Månsson, W., Colleen, S., Löw, K., Mårdh, P.-A. & Lundblad, A.:
Immunoglobulins in urine from patients with ileal and colonic conduits and reservoirs.
Submitted for publication.
- VI** Månsson, W., Colleen, S. & Mårdh, P.-A.:
Urine from continent caecal reservoirs. Studies on chemical composition and bacterial growth.
In manuscript.
- VII** Månsson, W., Colleen, S. & Mårdh, P.-A.:
The microbial flora of the continent caecal urinary reservoir, its stoma and the peristomal skin.
Submitted for publication.

These papers are referred to in the text by their Roman numerals, **I-VII**.



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Urinary diversion remains a major surgical procedure. Early and late complications have plagued every method used for diversion. The consequences of disrupted integrity of the urinary tract for renal function, the preservation of which is a sine qua non for success, are complex and should weigh heavily in the evaluation of methods for diversion. Established methods of urinary diversion are encumbered with several drawbacks which may adversely affect the patient's life. Renewed interest has therefore been shown in alternative diversion techniques which better accommodate patients' individual wishes.

Indications for urinary diversion

In deciding the most suitable method for urinary diversion in individual patients, the nature of the underlying disease is an important consideration.

Carcinoma of the urinary bladder requiring cystectomy is currently the most common indication for diversion of urine. In high-grade, invasive bladder carcinoma, radiotherapy often is an integral part of the treatment. But radiotherapy may additionally affect other organs in the small pelvis, including the most distal part of the ureters, the rectum and lower sigmoid region, and sometimes also the distal ileal segment, thereby influencing the choice of diversion procedure. Surgery on irradiation-damaged structures carries a high complication rate (Daughtry, Susan, Stewart & Straffon, 1977; Månsson, Colleen & Stigsson, 1979). This problem is increased when cystectomy ("salvage cystectomy") and urinary diversion are undertaken after "full-dose" radiotherapy. In patients with far advanced urothelial malignancy, palliative diversion of urine may be necessary to relieve pain and urgency of micturition. A simple method of diversion is advisable in such cases.

The incidence of bladder cancer is increasing. In Sweden the age-standardized incidence of urothelial malignancy per 100 000 men thus increased from 14.8 in 1960 to 26.2 in 1979 (Swedish Cancer Registry, 1982). If this trend continues, a rising number of patients may in the future face the need for urinary diversion, provided that principles of treatment remain unchanged.

Some patients with neurogenic bladder disorder may require urinary diversion. However, increased knowledge of neurovesical dysfunction, advances in uropharmacology and the introduction of clean intermittent self-catheterization and of artificial sphincters have contributed to a conservative attitude in these conditions, and resort to urinary diversion is uncommon nowadays. The possibility of concomitant disturbances in bowel and anal function must be considered in patients with neurogenic bladder disorder.

In children, neurogenic bladder disorders and certain congenital anomalies associated with urinary incontinence are indications for urinary diversion. For a review of this subject, readers are referred to Rickwood (1982). The following presentation does not deal with children.

The patient's age, physical fitness and comprehension are factors to be considered in decisions concerning method of urinary diversion, as should also be the patient's aesthetic requirements and social circumstances. These latter factors, however, have frequently been disregarded, partly due to focusing on the disease for which diversion is undertaken, and partly due to lack of acceptable alternative methods of diversion.

Established methods of urinary diversion

Within few fields of surgery has greater ingenuity been exercised than in the methods devised for diversion of urine. Since the first report on such a procedure (Simon, 1852), the urine stream has been conveyed to the outside of the body according to an indefinite number of surgical techniques (for a historical review cf Hinman & Weyrauch, 1936 and Murphy, 1972). The practicability of the described techniques has seldom corresponded to their theoretic advantages, and only a few have been accepted for clinical use.

Ureterosigmoidostomy

Ureterosigmoidostomy was the most commonly used method of urinary diversion up to the 1950s and 1960s, when several reports disclosed a high incidence of early complications and, at follow-up, of repeated pyelonephritic bouts, renal stone and loss of renal function (Jacobs & Stirling, 1952; Strömbeck, 1954; Clarke & Leadbetter, 1955; Riches, 1967). Reports on electrolyte disturbances contributed to the growing dissatisfaction with this type of diversion (Ferris & Odel, 1950; Stamey, 1956). Ureterosigmoidostomy therefore was almost abandoned. During the past decade, however, concomitant with a general realization that the ileal conduit, discussed below, is not the problem-free diversion it was once thought to be, there has been a renewal of interest in ureterosigmoidostomy. Strict indications for diversion, careful anti-reflux technique for the ureteral implantation and regular check-up with control and adjustment of the metabolic situation have improved results concerning renal function (Zincke & Segura, 1975; Bakker, Damme & Voogt, 1976; Marberger & Straub, 1982).

An increased incidence of colonic carcinoma arising at the ureterocolonic anastomosis has been reported in these patients (Urdaneta, Duffle, Creevy & Aust, 1966; Stewart, Macrae & Williams, 1982). As the latency averages 20 years (Rivard, 1975), this possible complication is of greatest concern in young patients with long life-expectancy, and it should necessitate regular colonoscopy surveillance.

Provided that the anal sphincter is competent, ensuring complete continence, ureterosigmoidostomy is aesthetically unsurpassed by the other methods of urinary diversion. This requirement is not always met, however, and it has been pointed out that the patients commonly have high frequency of bowel emptying and incontinence of fluid faecal material, which considerably restrict their daily lives (McConnell & Stewart, 1975; Macfarlane, Lattimer & Hensle, 1979). Children seem to achieve better anal sphincter control than do adults, and some authors have reported satisfactory "quality of life" for young patients (Aaronson & Morgan, 1979; Marberger & Straub).

Because radiation proctitis is common in patients subjected to radiotherapy of the small pelvis, ureterosigmoidostomy is not advisable for most patients undergoing cystectomy for cancer.

Conduit urinary diversion

Since the popularization of the *ileal conduit* in the 1950s (Bricker, 1950; Bricker, Butcher & McAfee, 1954), this method has largely replaced ureterosigmoidostomy, and today it is by far the most commonly used method for urinary diversion. Vast experience of ileal conduit has been gained, and in most cases the procedure is safe and yields acceptable results. It has become increasingly clear, however, that also this method suffers from serious long-term complications, notably renal deterioration (Murphy & Schoenberg, 1967; Schmidt, Hawtrey, Flocks & Culp, 1973; Stanley, Craven, Skinner & Richie, 1975; Middleton & Hendren, 1976; Dunn, Roberts, Smith & Slade, 1979; Pitts & Muecke, 1979; Månsson et al., 1979; Philp, Williams & Byers, 1980; Orr, Shand, Watters & Kirkland, 1981).

The *colonic conduit*, introduced in the 1960s (Turner-Warwick, 1960; Mogg, 1965), has increasingly come into use and is now considered an important alternative to the ileal conduit. The reason is the improved possibility for anti-reflux ureteral implantation. Although the sigmoid colon is most often used, a

conduit can be constructed from the transverse colon, which offers the advantage of being outside the target field for preoperative irradiation in bladder cancer (Beckley, Wajzman, Pontes & Murphy, 1982).

The *jejunal conduit* has been shown to entail a considerable risk of electrolyte disturbances (Golimbu & Morales, 1973; Månsson & Lindstedt, 1978), and its use is not advisable if other intestinal segments are available.

Cutaneous ureterostomy

This method is used mostly in children and as a palliative procedure in patients with advanced bladder malignancy. In certain cases it can be combined with a transureteroureterostomy with satisfactory results (Obrant, 1957; Lindstedt & Månsson, 1983). Stricture of the cutaneous stoma is a well-known complication, which limits use of this method to cases with dilated ureters.

Problems associated with a wet abdominal urostomy

Although most patients readjust well after construction of a wet urostomy and learn to accept the constant presence of an external appliance for collection of urine, a wide range of problems can occur. Despite considerable improvement in the quality and ease of handling of collecting appliances, and training of nurses in stoma care, complications from the stoma remain common in conduit urinary diversion. Such complications may secondarily affect the patient's lifestyle and sometimes also cause emotional problems. These aspects of urinary diversion have increasingly attracted interest.

The parameters used when reporting problems inherent in stomas and appliances are poorly defined, and the literature reflects extremes in this respect. The incidence of stoma stenosis in adults thus ranges from nil (Månsson et al., 1979) to 20 per cent (Murphy & Schoenberg), and for children even higher figures have been given (Middleton & Hendren). Stoma stenosis can impede drainage of the conduit and the upper urinary tract. It is often a consequence of various parastomal affections. These include dermatitis, ranging from reddened, weeping areas to hyperkeratotic skin lesions, acanthosis and ulcerations. Mentioned causal factors include flush stoma, allergic reaction to or poor fit of appliances and alkaline urine (Jeter & Lattimer, 1974; Jeter, 1976; Lawson, 1982). These complications jeopardize adherence of the plate of the appliance to the skin and thus entail risk of urine leakage.

Attempts have been made to eliminate the stomal problems by use of alloplastic materials as stoma prosthesis. An example is Biocarbon® (Bentley Laboratories, Irvine, USA), which is a carbon polymer in vitreous form. The main problems in the limited clinical trials have been encrustation, urinary fistula and staphylococcal infection (Månsson, Harzmann, Pow-Sang, Kobashi, Colleen & Raible, 1982). Further developmental work is necessary before the place of such materials in clinical practice can be determined.

The impact of a wet stoma on the patient's life can be considerable, the more so if stomal complications are present. Psychosocial problems due to change in the patient's perception of his "body image", and the presence of an appliance with risk of odour and leakage can restrict social contacts and cause professional disability and problems of sexual relationships (Tilma, Christensen & Fuglsang, 1973; Dunn et al.; Jones, Breckman & Hendry, 1980; Studer & Furger, 1981). These difficulties can add severe burdens to the patient's often deep-seated and far-reaching anxieties concerning the possibilities of recurrent malignancy.

Continent urinary diversion

Requirements

To obviate the problems associated with appliance-requiring urinary diversion, interest in the past decade has increasingly focused on continent diversion with achievement of voluntary control over the urine stream. The theoretic advantages over conventional methods of diversion are of aesthetic, psychologic, socio-economic and possibly also physiologic nature. For acceptance of continent urinary diversion in clinical practice, the following requirements must be fulfilled.

1. Adequate storage capacity for urine.
2. A reliable mechanism for continence, allowing voluntary easy and complete emptying of urine.
3. No endangering of renal function.
4. No metabolic disturbances due to transmucosal electrolyte shifts.
5. No deleterious nutritional effects produced by exclusion of the intestinal segment to be used for storage of urine.

The concept of collecting and storing urine in an excluded part of the intestine emerged as early as the turn of this century. Different parts of the gastrointestinal tract have since been used as reservoir for urine.

Rectal bladder

Perineal pull-through methods involve separation of the urinary and the faecal stream. The ureters are anastomosed to an isolated rectal pouch and the sigmoid colon is brought through the anal sphincter to open anterior or posterior to the anus (Gersuny, 1898; Heitz-Boyer & Hovelacque, 1912; Lowsley & Johnson, 1955; Duhamel, 1959; Nédélec, 1967; Bracci, 1968; Tacciuoli, Laurenti & Racheli, 1977). The prospect of voluntary sphincter control over emptying and the position of the outlet are attractive features, and in these respects the rectal bladder is superior to a urinary reservoir with abdominal stoma. However, the intricate technique and the questionable continence have contributed to an indifferent attitude from most urologists. A simpler variant, the rectal bladder combined with an abdominal colostomy (Mauclaire 1895) has gained popularity in centres dealing with Bilharzia-induced squamous cell carcinoma of the bladder. But in these patients too incontinence has been a problem (Ghoneim, Shehab-El-Din, Ashamallah & Gaballah, 1981). In western-world countries, the adjuvant radiotherapy given to most patients with bladder carcinoma makes these methods unsuitable.

Urinary reservoirs with abdominal stoma

Such constructions have no sphincter mechanism under voluntary control. A continence-providing mechanism in the outlet must therefore be arranged. This mechanism must allow easy insertion of a catheter at regular intervals for emptying of the reservoir. A small stoma, covered only with a gauze pad, is desirable. Most experience has been gained with reservoirs constructed from caecum or from ileum.

The continent caecal reservoir. Since the early years of this century the caecal or ileocaecal segment has been used in attempts to accomplish continent

urinary diversion (Verhoogen, 1908; Makkas, 1910; Gilchrist, Merricks, Hamlin & Rieger, 1950; Sullivan, Gilchrist & Merricks, 1973; Ashken 1974; 1978; 1982; Benchekroun, 1977; 1982; Månsson & Sundin, 1977; 1978; I; Zingg & Tscholl, 1977; Vrabel, 1981). The ileocaecal segment has also been used as a urinary conduit (Libertino & Zinman, 1982) and has gained popularity as a suitable segment for use in urinary bladder augmentation (Gil Vernet, 1960; Turner-Warwick & Ashken, 1967). Certain characteristics of the caecum make it suitable as a reservoir; it has a large diameter and is seldom involved in colonic diseases such as diverticulosis. However, several aspects of a caecal reservoir for urinary diversion are as yet incompletely understood.

The continent ileal reservoir. An ileal reservoir for gastrointestinal contents in proctocolectomized patients was devised by Kock and colleagues in Gothenburg and has gained acceptance (Kock 1969; 1971; Kock, Darle, Hultén, Kewenter, Myrvold & Philipson, 1977; Kock, Myrvold, Nilsson & Åhrén, 1980). The same principle, resembling one described by Blandy (1961) for construction of a bladder substitute, was used to create a urinary reservoir (Norlén, Kock, Nilson & Sundin, 1975; Leisinger, Säuberli, Schauwecker & Mayor, 1976; Madigan, 1976; Trasti, 1978; Kock, Nilson, Nilsson, Norlén & Philipson, 1982; Gerber, 1983). Briefly, 60–70 cm of the small bowel is isolated 50 cm from the ileocaecal sphincter, and 40 cm of the isolate is folded into a U, the legs of which are sutured together. The intestine is then split open at the antimesenteric border. By folding the intestinal plate a pouch is achieved (Fig. 1). An elaborate technique thus is necessary to create an adequate volume-holding pouch.

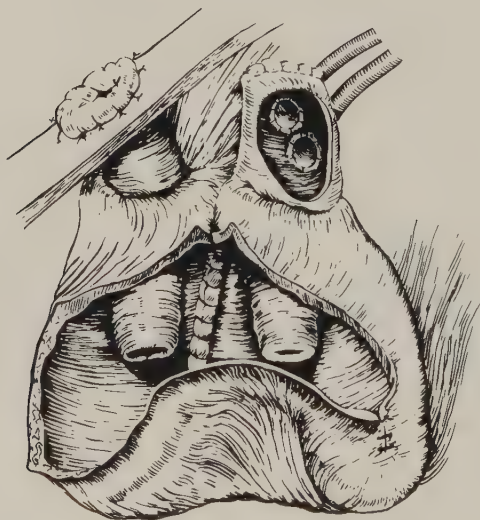


Fig. 1. The ileal reservoir for urine (Kock et al.).

The continent caecal reservoir for urine

Aims of the study

To evaluate the usefulness of a continent caecal urinary reservoir in clinical practice as an alternative to other methods, answers to the following questions were judged to be important:

1. Does construction of a continent caecal reservoir for urine carry high postoperative morbidity?
2. Does the exclusion of an ileocaecal segment adversely affect nutritional processes? Does electrolyte disturbance arise from electrolyte shift across the caecal mucosa?
3. Is adequate functional capacity of the reservoir attainable?
4. Can a reliable mechanism be provided to ensure continence and ease in catheterization?
5. Will reservoir distension influence the upper urinary tract?
6. What is the optimal method for ureterocaecal anastomosis?
7. What is the long-term outlook for renal function?
8. Is urinary tract infection (UTI) common in patients with caecal urinary reservoir, and what is the microbial pattern?
9. Does the chemical composition of urine from patients with caecal reservoir favour the establishment of UTI?
10. Which mechanisms may be important for protection of these patients against UTI?

Patients

In attempts to accomplish continent urinary diversion, caecal reservoir was constructed in 18 patients in the period 1977–1982. The indication for diversion in all cases was high-grade, invasive carcinoma of the bladder. A staged treatment procedure was used in most of the patients. The caecal reservoir thus was first constructed. Three or four weeks later preoperative pelvic irradiation was begun, and after its termination cystourethrectomy was performed (I).

Of the 18 patients, 15 are alive and have been followed up for periods ranging from 18 to 79 months. Two of the three deaths were caused by metastatic disease. The third death occurred from complications which followed the cystourethrectomy, performed in a second session, and were unrelated to the diversion procedure.

Surgical procedure

Construction of the caecal reservoir involved isolation of the distal 20 cm of ileum, the caecum and part of the ascending colon (I). Bowel continuity was restored by ileocolic anastomosis. The appendix was removed. The ureters were implanted with anti-reflux technique. The continence-providing principle was an intussuscepted ileal nipple valve, constructed from the distal part of the ileum. As experience was gained, the technique was modified to enhance stability of the nipple valve. The ileum was brought out through the rectus muscle below and to the right of the umbilicus, redundant ileum was excised and a stoma was fashioned flush with the skin (Fig. 2).

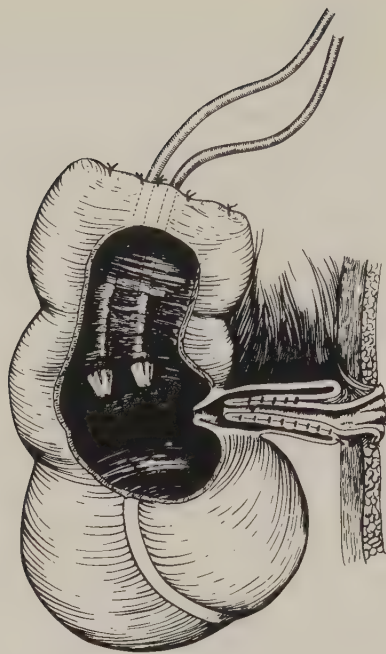


Fig. 2. The caecal reservoir for urine, present version (Månsson et al.).

The reservoir-draining catheter was removed after three weeks, and the patient was instructed in the technique of clean intermittent self-catheterization with progressively longer intervals, using a plastic catheter 24F (Medena®, Astra-Meditec, Mölndal, Sweden) or a Foley-type silicone catheter. Between catheterizations the stoma was covered only with a gauze pad or a Hollister Stoma Cap® (Abbott).

Postoperative complications occurred in three patients (I). In one of them, bowel obstruction and insufficiency of the intestinointestinal anastomosis necessitated resection of small and large bowel. Urine leakage, probably from the caecal suture line, in a second patient and impaired circulation to the stoma due to compression of the mesentery in a third patient also required surgery. There were no deaths associated with reservoir construction. In the other 15 patients the postoperative course was uneventful.

A caecal reservoir for urinary diversion is more time-consuming to construct than a conduit. When performed in the management of disease requiring cystourethrectomy, construction of a caecal urinary reservoir constitutes major surgery. A higher risk of complications may be inherent in this type of diversion. The types of complications here reported can occur also after conduit diversion. They do not, as such, seem prohibitive for the construction of a caecal reservoir.

Properties of the ileocaecal segment

Nutrition and serum electrolytes

Exclusion of an ileocaecal segment from the gastrointestinal tract and its positioning within the urinary tract is a potential cause of nutritional and electrolyte disturbances.

The loss of the ileocaecal sphincter entailed in construction of continent caecal reservoir may affect transit time of the intestinal contents. This change may have clinical significance if major resection of the distal small bowel also is performed, giving rise to diarrhoea and malabsorption (Wright & Tilson, 1973; Cosnes, Gendre & Le Quintrec, 1978). In one patient of the series here presented, resection of the small and the large bowel was done because of postoperative complications. Diminution of serum cobalamin was found two years later, and he has since been treated with vitamin B₁₂. In the other patients, the serum cobalamin and folic acid levels have remained normal.

When any gastrointestinal segment is positioned in the urinary tract, shifts of crystalloid substances and water occur across the mucosa. Kidneys with normal function can compensate for these shifts. Absorption of electrolytes and urea is smaller and slower from a colonic segment than from an ileal or a jejunal segment (Madsen, 1964; Janknegt, 1967; Genster, 1971). Bicarbonate ions are secreted across the colonic mucosa in exchange for chloride ions (Madsen), which may explain the raised and stable pH found in caecal reservoir urine (VI). A high pH makes the urine a more favourable medium for bacterial growth. In patients with caecal reservoir the 24-hour urine volume emptied from the reservoir was higher than in subjects with intact urinary tract (VI). This may be attributable to flux of water along the osmotic gradient across the caecal mucosa (Phillips & Summerskill, 1967).

A slight reduction in base excess was found in two patients in the present series (VI). Slightly raised serum chloride and lowered serum bicarbonate have been reported in patients with caecal urinary reservoir (Ashken, 1982) and patients with ileocaecal cystoplasty and reduced renal function were observed to have hyperchloraemic acidosis (Whitmore & Gittes, 1983).

Exclusion of the small-bowel segment required for the construction of an ileal reservoir for urine should not cause interference with the absorption of bile salts and vitamin B₁₂. Shifts of electrolytes and water across the mucosa occur also with an ileal reservoir (Jagenburg, Kock, Norlén & Trasti, 1978). Metabolic acidosis in the presence of reduced renal function has been observed also with this method of diversion (Gerber).

Little risk of nutritional disturbance seems to be entailed by the exclusion of the ileocaecal segment required to construct a continent caecal reservoir for urine. However, additional extensive small-bowel resection is poorly tolerated and may cause diarrhoea and malabsorption. When renal function is normal, changes in serum electrolyte and acid-base balance associated with caecal urinary reservoir are unlikely to be clinically significant. If there is renal insufficiency, however, hyperchloraemic acidosis may appear.

Functional capacity

A continent caecal reservoir for urine provides adequate volume-capacity. The patient empties the reservoir at intervals of three to five hours, and as a rule once nightly. When the reservoir is full, a slight cramp-like sensation is experienced, which indicates to the patient that the reservoir should be emptied. The sensation is produced by intrareservoir pressure waves, which occur every second or third minute with a full or near-full reservoir. The amplitude of the pressure waves increases with increasing filling. Thus, at a volume of 500 ml or more, the amplitudes may reach over 50 cm H₂O (II). In the course of time after construction of the caecal reservoir, the amplitude of the pressure waves diminishes, indicating increase in functional capacity (II). Between the waves a low basal pressure is present (Ashken, 1982; II).

The advantage of the ileal reservoir over the caecal reservoir has been claimed to be low pressure in the former (Kock et al., 1982), achieved via the special orientation of the intestinal flaps, supposedly cancelling out the motor activity (Ekman, Jacobsson, Kock & Sundin, 1964). This effect has been questioned, however (Cranley & McKelvey, 1983). The pressure in an ileal reservoir for intestinal contents was reported to exceed 50 cm H₂O when full (Akwari, Kelly & Phillips, 1980), and in ileal urinary reservoir pressure waves with amplitudes up to 35 cm H₂O were registered (Norlén & Trasti, 1978).

Caecum used as a reservoir for urine, offers a capacity for collection and storage that gives emptying intervals convenient for the patient.

Continence-providing principle

The major obstacle to successful construction of continent urinary reservoirs has been to obtain a reliable continence-providing mechanism for the reservoir outlet. Numerous variants have been tried.

The intussuscepted ileal nipple valve

This type of valve, described by Perl in 1949, was later used experimentally to prevent ascending infection after uretero-ileal-sigmoid anastomosis (Basso, 1951) and clinically as the intussuscepted ileal cystostomy to prevent leakage of urine (Smith & Hinman, 1955). It was reappraised by Kock (1971) for achievement of a continent ileal reservoir after proctocolectomy. The intussuscepted ileal nipple valve has been used both as the continence-providing principle and as the reflux-preventing principle (Fig. 1) in the *ileal urinary reservoir* (Norlén et al.; Leisinger et al.; Madigan; Kock et al., 1982; Gerber). The same type of valve has been used for achievement of continence in the *caecal urinary reservoir*. An ileal nipple valve was fashioned to protrude through the ileocaecal sphincter into the caecal cavity (Fig. 3) (Månsson & Sundin, 1977; 1978; I; Zingg & Tscholl; Vrabel). Difficulties in catheterization and leakage of urine soon arose, however, due to nipple valve malfunction (Månsson & Sundin, 1978; I; Zingg, 1978).

The main problem with the intussuscepted ileal nipple valve is the valve's tendency to slide. This process starts at the mesenteric side, where the two layers of the valve cannot be fixed to each other because of intervening mesentery. Sliding leads to incontinence and difficulties in inserting the catheter. Prolapse of the nipple valve may also occur. Inadequate fixation of the

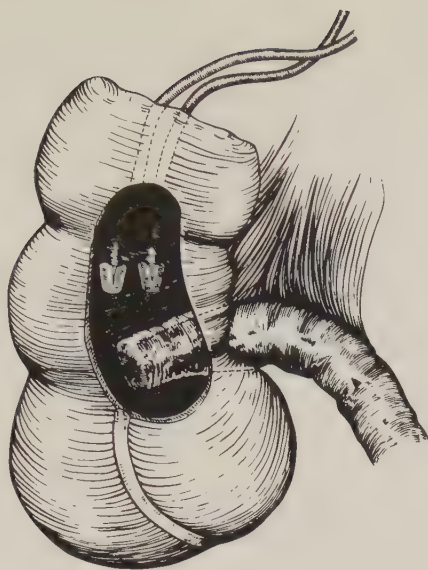


Fig. 3. The caecal reservoir for urine, initial version (Månsson et al.).

nipple base to the abdominal wall can cause angulation of the outlet and difficulties in catheterization. These problems have been common with both ileal and caecal urinary reservoir (Kock et al., 1982; **I**) and have necessitated revisional procedures in a substantial number of patients.

The root cause of reservoir outlet malfunction lies in the dynamics of the reservoir and its outlet. Intermittent high-pressure waves may affect the nipple valve directly and give rise to prolapse. The reservoir wall tension that generates the high intrareservoir pressure has been ascribed causal significance for the sliding process, as it tends to tear the two layers of the nipple apart (Norlén & Trasti). In simultaneous measurement of the pressure in the reservoir and in the nipple valve, differences were found between patients with continent caecal reservoir who never experienced urinary leakage and those with risk of leakage at high filling (**II**). The prerequisite for continence of a reservoir, i.e. higher intraluminal pressure in outlet than in reservoir, was present in both groups, but in the latter the outlet pressure waves sometimes peaked later than the simultaneously initiated pressure waves in the reservoir. Possibly it can be explained by sliding of the bowel layers of the nipple valve, with the peak of the pressure not being reached until the sliding process stops (**II**). This delay implies risk of negative closure pressure with concomitant leakage of urine. In between the reservoir contractions, leakage is prevented by a higher basal pressure in the ileal outlet than in the reservoir. However, in incontinent patients, no high-pressure zone was detectable in the reservoir outlet (**II**).

Measures to improve valve stability. To counteract the influence of reservoir pressure and wall tension on the nipple valve, various measures to improve stability have been tried. In addition to deperitonealization of the mesentery, removal of fat between the mesenteric vessels and electrocautery as suggested by Kock (1973; Kock et al., 1977), the 4–5 cm long nipple valve was positioned within the distal ileum just proximal to the ileocaecal valve and several rows of silk sutures were placed between the serosal surfaces (**I**) (Fig. 4). The intact ileocaecal sphincter was expected to reduce the negative influence of intrareservoir pressure on the nipple valve. Some observations seemed to

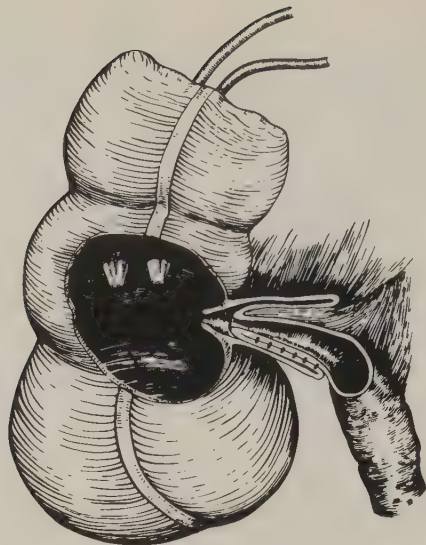


Fig. 4. The caecal reservoir for urine, second version (Månsson et al.).

support this assumption. Thus, a 4 cm long zone with intraluminal pressure higher than in colon was demonstrated at the ileocaecal junction, responding with increasing pressure to colonic distension (Cohen, Harris & Levitan, 1968). Although the results as regards continence were improved, these valves were incompetent in some patients, with ensuing leakage or difficulties in catheterization (I).

Another modification was therefore made, viz. mesenterial exclusion as suggested by Hendren (1980), which enables the placing of silk sutures circumferentially along part of the nipple valve (Fig. 5). This measure was shown experimentally to improve stability of the nipple valve (Cranley & McKelvey, 1981). This technique gave stable nipple valves and all five surviving patients have been continent. In three of them, however, difficulties in catheterization required reoperation. The nipple base was found to be inadequately fixed to the abdominal wall. This caused angulation of the outlet, part of which seemed to have been transformed into a blind pouch by repeated pushing with the catheter. It is notable that the nipple valve was symmetric without sliding tendency, but the tip of the nipple showed signs of deficient blood supply – pallor and fibrosis of the bowel wall (I). These observations illustrate the importance of a limited mesenterial occlusion and of careful fixation of the nipple base to the abdominal wall.



Fig. 5. The intussuscepted ileal nipple valve with mesenterial exclusion, present version (Månsson et al.).

Other suggested measures to reduce the risk of sliding of the valve were use of a stapling instrument (Steichen, 1977) and placement of a strip of Marlex® mesh or fascia around the nipple base, passing through the mesentery and sutured to the nipple base and the abdominal wall (Kock et al., 1980). The strip would also ensure a straight course of the outlet, diminishing the risk of the nipple base loosening from the abdominal wall.

Alternative continence-providing principles

The possibilities of other continence-providing mechanisms of the caecal reservoir were explored by Ashken (1974; 1978; 1982) and Benckekroun (1977; 1982). In his first patients, Ashken constructed an everted "spout valve" on a separate ileal isolate, which was sutured into the open end of the caecum. The main problem with this method was prolapse of the valve. This occurred also when the ileal spout valve was placed through the ileocaecal sphincter. The next variant was simply to insert one end of the ileal isolate into the open end of the caecum as a "flutter valve" and suture it along the lateral wall of the caecum (Fig. 6). Urinary fistula has formed where the mesentery of the ileal isolate runs into the caecum. Interestingly, spontaneous eversion of the "flutter valve" into a "spout valve" has been observed. Functional results, however, i.e. continence and ease of catheterization, were improved with the flutter variant. A drawback is that construction of this valve requires a separate bowel isolate. The same applies to the "inkwell valve" designed by Benckekroun, in which the principle of the "spout valve" is reversed. One end of the ileal isolate is invaginated to emerge from the other end, which is sutured to the open end of the caecal isolate (Fig. 7). Devagination of the valve has been a major problem. The exposed mesentery is "epithelialized" and has sustained no damage at catheterization (Benckekroun, 1982, personal communication).

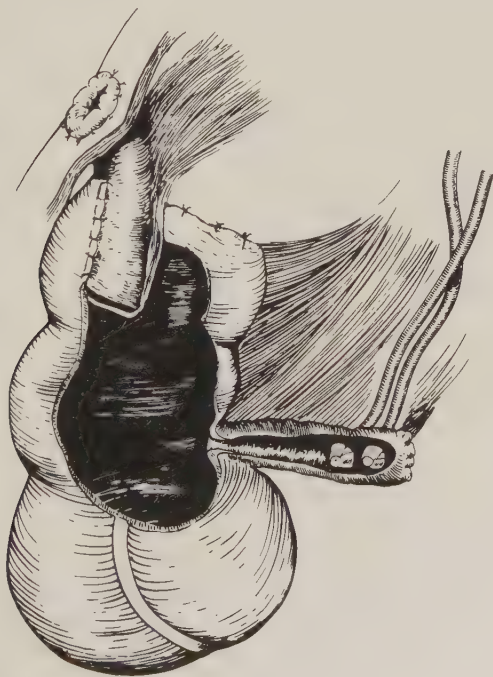


Fig. 6. The caecal reservoir for urine (Ashken).

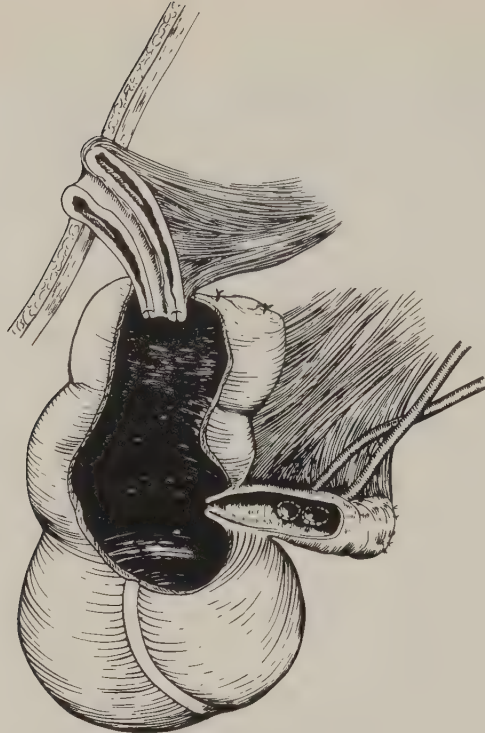


Fig. 7. The caecal reservoir for urine (Benckekroun).

Of historic interest only is the use of appendix as outlet (Verhoogen; Makas). Sporadic reports thereafter claimed that continence could be achieved through the action of Gerlach's valve at the base of the appendix, an oblique course through the abdominal wall and, sometimes, use of a truss covering the appendicostomy. But in the latest report on this method the patients were stated to be incontinent (Cortes, 1946). Reliance for provision of continence has further been placed on the ileocaecal sphincter and preserved peristalsis of a long ileal segment (Gilchrist et al.; Merricks & Gilchrist, 1957; Sullivan et al.). As early as 1908, however, Verhoogen observed that this principle for achieving continence seemed to be unreliable, and catheterization of the reservoir has proved to be difficult (Bricker, 1950; Bricker & Eiseman, 1950; Harper, Berman, Hertzberg, Lerman & Brendler, 1954; Brendler, 1974).

Functional results

To achieve continence and ease in catheterization of the caecal urinary reservoir, revision of the outlet had to be performed in most of the patients (I). Increased experience and modifications of the technique led to improved results, however. Of the 15 surviving patients, 12 are continent and empty their reservoirs at intervals of three to five hours. Occasional prolapse of the nipple valve necessitates use of a small stoma-covering truss in three cases. Also in other reported series, revision of the reservoir outlet was required in a substantial number of the patients to ensure a well-functioning reservoir (Ashken, 1982; Benckekroun, 1982; Kock et al., 1982). The dry stoma, freedom from appliances, intact peristomal skin and absence of odour obtained with a continent urinary reservoir are gratifying and encouraging, and in these respects render reservoir diversion superior to conduit methods. Patients who had other types of urinary diversion before an ileal reservoir considered the elimination

of appliances to be most advantageous (Kock et al., 1982). Patients with caecal reservoir similarly experienced temporary need of a collecting appliance, because of leakage, as a setback. Occasional difficulties in catheterization of the reservoir, however, were disconcerting to patients (I).

The surgical complexity of creating a stable, well functioning and continence-providing mechanism in the reservoir outlet, and the risk that revisional procedures may be required, make the selection of patients important. The best results are achievable in patients of slender physique, with a thin mesentery. The patient's cooperability and comprehension are important. Any sign of radiation injury to the small bowel precludes attempts to fashion an intussuscepted nipple valve, due to high risk of an imperfect union between the nipple walls.

With a caecal reservoir for urine, continence is achievable, eliminating need for external collecting appliances. A reliable intussuscepted ileal nipple valve is difficult to construct, however, and revisional procedures may be necessary. Experience of the method and selection of patients are important factors for success. The patient's potential gain in "quality of life" warrants further trials of this alternative method for urinary diversion.

Renal function after continent caecal urinary diversion

The influence of reservoir distension on the upper urinary tract

When the urinary bladder is full, dilatation of the upper urinary tract and rise in the renal pelvic pressure can occur even in the absence of vesico-ureteral reflux (Gill & Curtis, 1977; Kinn, 1981). As the pressure in the full caecal reservoir is intermittently high, this could conceivably damage renal function by impeding the urine flow. To investigate the influence of reservoir distension, scintillation camera renography was performed with empty and with full reservoir. Renograms obtained from different kidney regions in patients with caecal reservoir were compared with renograms recorded at empty and at full urinary bladder (III).

Whereas the renographic curves for parenchyma and pelvis with empty caecal reservoir were almost identical with corresponding records at empty urinary bladder, considerably delayed isotope passage in parenchyma and, especially, pelvis was observed in several patients with full caecal reservoir. Fullness of the urinary bladder, by contrast, exerted little influence on the passage of isotope through the kidney (III). Appreciable differences between the renogram curves from the two kidneys were found at full bladder/reservoir, indicating that the shape of the uretero-vesical junction/ureteral implantation may be more important than the pressure per se (III). Other authors reported a renographic picture of functional obstruction in patients with a full ileal reservoir (Åkerlund, Berglund, Granerus, Kock & Philipson, 1983). However, they found this picture only when high intrareservoir pressure accompanied fullness of the reservoir. Improved drainage of the upper urinary tract occurred in response to reduction of reservoir volume, and hence also of pressure. The conclusions were that a "low-pressure reservoir" is desirable, and that intervals between emptying should not be too long.

A full caecal urinary reservoir can cause functional obstruction to the flow from the upper urinary tract. The shape of the uretero-intestinal anastomosis may be important in this context. Obstruction probably is present only for short periods, as fullness of the reservoir is accompanied by slight cramp-like sensations, signalling to the patient that the reservoir should be emptied.

Method of uretero-caecal anastomosis

Obstruction of the uretero-intestinal anastomosis, which may influence renal function, is to some extent dependent on the type of the anastomosis. Simple anastomosis performed under visual control of the lumen thus may be advantageous (Sundin & Pettersson, 1974; Månsson et al., 1979). Conversely, techniques aimed at preventing reflux, such as a ureteric nipple in an ileal conduit or a long submucosal tunnel in a colonic conduit, may cause obstruction, partly because of their more elaborate formation (Feuk, Fritjofsson & Frödin, 1978; Dagen, Sanford & Rohner, 1980; Arap, Giron, Abrão, Mitre & de Góes, 1982).

As deterioration of the upper urinary tract may occur in patients with ileal conduit and no obstruction, free reflux of infected conduit urine has been blamed (Smith, 1972; Middleton & Hendren; Bergman, 1978; Rickwood). The use of colonic conduit with anti-reflux technique for the ureteral implantation has been considered to improve the outlook for renal function (Altwein, Jonas & Hohenfellner, 1977; Althausen, Hagen-Cook & Hendren, 1978). Because of the dynamics of the caecal reservoir, with intermittent high pressure, and the frequent occurrence of bacteriuria, anti-reflux implantation of the ureters was judged to be advantageous. The technique used (Fig. 8) was a combination of a submucosal tunnel (Goodwin, Harris, Kaufman & Beal, 1953) and a ureteric split-cuff nipple (Turner-Warwick & Ashken), and it has proved effective in preventing reflux (I). On the other hand, the fairly intricate procedure possibly is associated with enhanced risk of stenosis. Within a year of diversion stenosis occurred in 3 of 36 anastomoses (I). These strictures, which were short, were probably due to necrosis of the ureteric nipples, as they were not detectable at surgical revision.

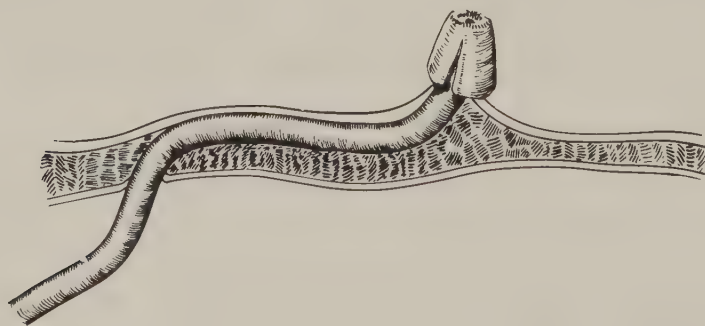


Fig. 8. The uretero-caecal anastomosis (Goodwin et al. + Turner-Warwick & Ashken).

Ashken (1982) relied on the ileocaecal sphincter and anti-reflux implantation of the ureters in the terminal part of the ileum to prevent reflux, whereas Benchekroun (1982) implanted the ureter with a direct technique in the same segment. The reflux reported in several of Benchekroun's cases testifies to the inability of the ileocaecal sphincter to prevent reflux.

In the ileal reservoir, a second intussuscepted ileal valve protects against reflux, and the ureters are implanted proximal to it, using a direct technique. Malfunction of this valve may occur, however. Incompetence with resultant reflux has been observed (Kock et al., 1982).

Anti-reflux uretero-caecal anastomosis is recommended in the construction of a continent caecal reservoir as there is intermittent high intraluminal pressure and bacteriuria.

Glomerular filtration rate at follow-up

After urinary diversion via a continent reservoir, the course of renal function is of utmost concern. It is also the parameter against which the introduction of such diversion types must be judged. New methods of urinary diversion in patients with long life-expectancy are not justified if they imply higher risk to the renal function than do established diversion procedures. Hence the logical comparison of renal function in patients with continent caecal reservoir is against renal function after conduit urinary diversion.

Serum creatinine and urography are conventionally used for evaluating renal function after urinary diversion. Both methods, however, are blunt tools for this purpose. Serum creatinine within normal range does not preclude impaired renal function (Brøchner-Mortensen, Jensen & Rødbro, 1977). The difficulties of judging the implications of urographic changes at follow-up of patients subjected to urinary diversion and the lack of defined parameters were stressed by Bricker (1980).

To achieve accurate assessment of renal function, GFR can be measured as plasma clearance of ^{51}Cr -EDTA, a test with high precision (Brøchner-Mortensen & Rødbro, 1976). As unilateral impairment of renal function with contralateral compensatory increase can present as unchanged total renal function, determination of separate renal function is of value. This can be done when scintillation camera renography also is employed (Duffy, Casey & Barker, 1982).

Plasma clearance of ^{51}Cr -EDTA and scintillation camera renography were used in addition to serum creatinine and urography in a prospective study comparing the course of renal function in patients with caecal reservoir or ileal or colonic conduit who were observed for periods of 24 to 67 months (IV). In the patients with conduit urinary diversion, one ureter had been implanted with anti-reflux technique and the other with direct, reflux-permitting technique. The total GFR showed a mean decrease of 10 per cent in the two conduit groups and was unchanged in the reservoir group. No difference in separate GFR was found between kidneys protected from reflux and those not protected in either conduit group (IV). Most patients with moderately decreased GFR had serum creatinine within normal range. The urographic appearance could be normal despite significant decrease in separate renal function. On the other hand, urography could show significant changes although renal function was well preserved (IV).

Follow-up urography of patients with caecal reservoir showed no or only minimal dilatation of the upper urinary tract, except when there was stricture of one of the uretero-intestinal anastomoses. This occurred in three patients. In one of them, complete loss of function of one kidney occurred. In the other patients, ureteral reimplantation resulted in no further renal deterioration in one and complete restoration of function in the other. Since then, separate

GFR in these two patients have been stable despite free reflux of infected urine for some years. Nor have they shown signs of pyelonephritis (IV). It is well known that reflux and infection of urine in patients with intact lower urinary tract entail considerable risk of loss of renal function (Fritjofsson & Sundin, 1966; Smellie, Edwards, Hunter, Normand & Prescod, 1975). This circumstance indicates presence of protective mechanisms in the urine from caecal urinary reservoirs.

Preserved renal function has been found also in other series of patients with continent urinary diversion (Benckekroun, 1982; Kock et al., 1982; Ashken, 1983, personal communication).

Renal function in patients with a caecal reservoir for urine is well preserved at long-term observation and compares favourably with the function in patients with conduit urinary diversion. The intermittent functional obstruction to urine flow that occurs when the reservoir is full had not influenced renal function after observation for on average three years. Diminution of renal function was found only when there was stricture of the uretero-intestinal anastomosis.

Urinary tract infection after continent caecal urinary diversion

Caecal reservoir urine as growth medium for bacteria

Physicochemical factors with proven influence on bacterial growth in urine are pH, osmolality and concentrations of urea and glucose. The pH and concentration of urea were found to differ between caecal reservoir urine and urine from persons with intact urinary tract (VI). Caecal reservoir urine had higher pH than normal urine and, unlike the latter, this pH changed very little over 24 hours. High pH has been found also in ileal reservoir for urine (Jagenburg et al.). Such pH is favourable for bacterial growth (Asscher, Sussman, Waters, Davis & Chick, 1966; Kaye, 1968). A high urea concentration inhibits bacterial growth (Kaye). Reservoir urine was found to have lower urea levels than normal urine, probably caused by a higher 24-hour urine output in patients with reservoir. The albumin level was higher in reservoir urine than in urine from controls. When bacterial growth rate was studied, however, no major difference was found between caecal reservoir urine and normal urine as regards *Escherichia coli*, species of *Proteus* or *Pseudomonas* at any pH (VI). This indicates that caecal reservoir urine presumably is equivalent to normal urine as a culture medium.

Secretory substances in the host defence against urinary tract infection

A mucosa with preserved secretory functions may be important for production of substances such as immunoglobulins, mucin, lysozymes and enzymes, which may act as mucosal defence mechanisms. The caecal mucosa seems resistant to urine. Scanning electron microscopy (Fig. 9A, B) and light microscopy (Fig. 10) showed normal morphology of the caecal mucosa some years after construction of caecal reservoir. An analogous observation was made in a caecal reservoir of Makkas type 43 years after its construction (Bjersing, 1963). Contrarily, urine seems to be noxious to the ileal mucosa, and mucosal atrophy to complete avillar areas has been noted in ileal reservoirs for urine (Philipson, Kock, Jagenburg, Åhrén, Norlén, Robinson & Menge, 1983).

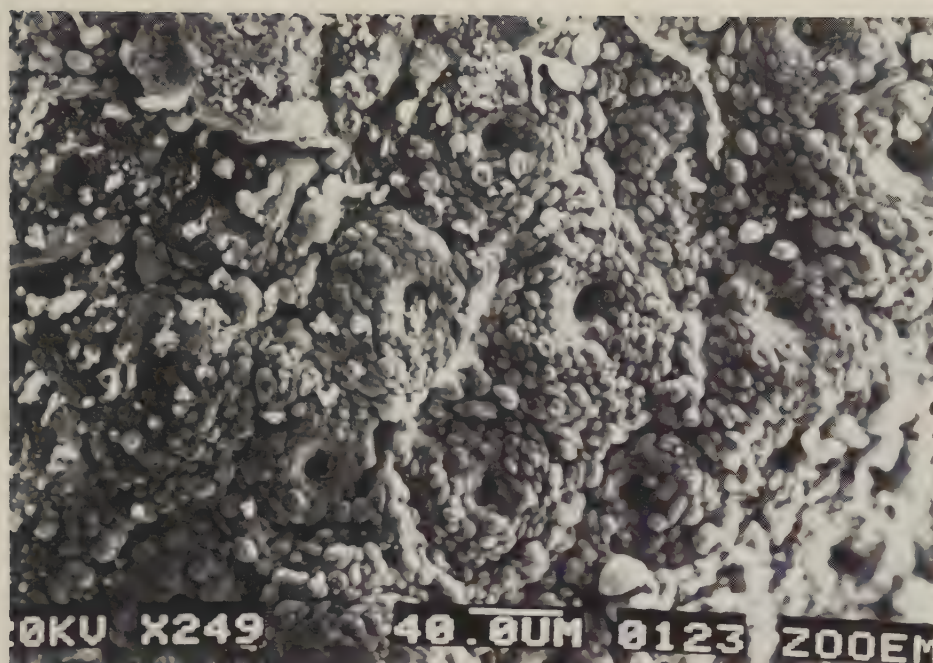


Fig. 9A. Scanning electron micrograph of mucosa from caecal reservoir for urine in a 55-year-old man, 68 months after construction. The mucosal surface is regular with clearly visible crypt openings.

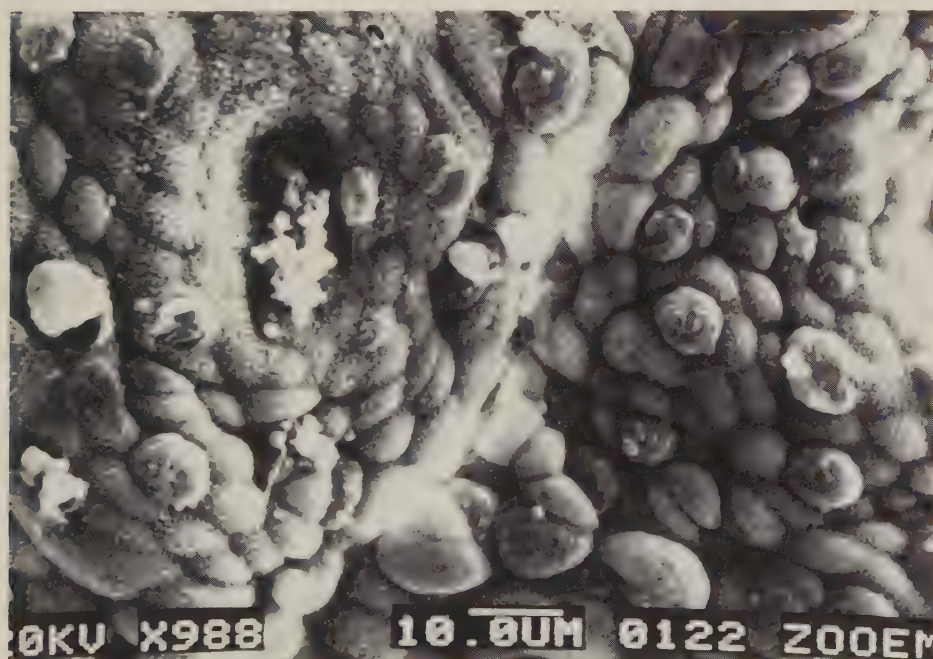


Fig. 9B. Higher magnification of Fig. 9A. The enterocytes have well defined borders and preserved microvilli.



Fig. 10. Light micrograph of mucosa from the same caecal reservoir as in Fig 9. The crypt structures are preserved with normal amounts of goblet cells. In the lamina propria there is slight fibrosis and slightly increased number of inflammatory cells ($\times 80$).

Immunoglobulins. These proteins, among which secretory IgA (sIgA) predominates, may contribute to the host defence at the mucosal surfaces of the body. sIgA has been shown to prevent adherence of bacteria to such surfaces (Williams & Gibbons, 1972; Fubara & Freter, 1973). In a study of the gel chromatographic distribution of proteins in urine from healthy persons with intact urinary tract and from patients with caecal reservoir, the latter urine was shown to contain large amounts of high molecular weight proteins, especially sIgA (V). Quantitation of immunoglobulins, using electroimmunoassay and single radial immunodiffusion, showed that urine from ileal and colonic conduits and from ileal and caecal reservoirs contained considerably more sIgA, IgG and IgM than did urine from individuals with intact urinary tract (V). More sIgA was found in reservoir urine than in conduit urine, but there was no such difference for IgG or IgM. The difference in sIgA thus could not be explained on the basis of differences in the mucosal surface area. Factors such as difference in antigen stimulation, due to differential patterns of infection in reservoirs and conduits, may be of importance. The differing intestinal segments used in the various procedures did not seem to influence the results. Nor was there any correlation between the number of bacteria in caecal reservoir urine and the amount of sIgA (V).

IgA antibodies from caecal reservoir urine were found to inhibit mannose-resistant haemagglutination by *E. coli* from caecal urine (V). Substances known to inhibit such agglutination are known also to inhibit adherence of the bacteria to eukaryotic mucosal cells. The presence of sIgA in caecal reservoir urine thus may prevent bacterial adherence to the caecal mucosa. No mucosa-attached bacteria were found on scanning electron micrographs of the caecal mucosa (unpublished observations). Haemagglutination-inhibition was found also in

tests with *E. coli* from faecal samples (V). This may support the theory of the common mucosal immune system (Bienenstock & Befus, 1980), i.e. circulating plasma cells that are committed to production of IgA antibodies home also to mucosal surfaces which are not stimulated by the antigen.

Mucin. Abundant mucin production persisted years after construction of a caecal reservoir, and light microscopy showed normal amounts of goblet cells (Fig. 10). Mucin may be important in protecting the mucosal surface against infection by preventing bacterial colonization, i.e. by functioning as receptor analogues (Svanborg Edén, Freter, Hagberg, Hull, Hull, Leffler & Schoolnik, 1982).

The microbial flora

Urine from caecal reservoir persistently showed growth of aerobic or facultatively anaerobic organisms in a few patients (VII), while in most of the others these organisms were only occasionally isolated. As a rule, they were isolated in pure culture. Similar findings were common in colonic conduit urine, but not in ileal conduit urine (Hill, Hudson & Stewart, 1983). In caecal reservoir urine, obligate anaerobes were found only in conjunction with facultative anaerobes.

Persistent or intermittent bacteriuria has been found in most patients with caecal or ileal urinary reservoir (Ashken, 1982; Benchekroun, Lakrissa, Tazzi, Mikou & Abakka, 1982; Philipson, Brevinge, Kock, Norlén, Åkerlund & Öjerskog, 1983). Bacteriuria is common also in patients with intact lower urinary tract in whom clean intermittent catheterization is used (Lapides, Diokno, Gould & Lowe, 1976; Ehrlich & Brem, 1982). It is possible that contamination at reservoir catheterization plays a role in establishing bacteriuria. There seems to be a connection between bacteriuria and the number of bacteria present at stoma level (VII). In persons with intact urinary tract and susceptibility to urinary tract infection (UTI), abnormal periurethral colonization often precedes episodes of infection (Stamey, Timothy, Millar & Mihara, 1971; Bollgren & Winberg, 1976). Similarly, in patients with continent urinary reservoir the importance of overcoming the "infectious dose" in the distal part of the new urinary tract must be considered in the establishment of UTI in these patients. A well-functioning nipple valve may function as an ecologic barrier against colonization of the reservoir. Thus, persisting growth of bacteria was found in patients with risk of urine leakage at high filling of the reservoir, e.g. the nipple valve function was not perfect (VII).

Antibiosis. In in vitro experiments (VII), bacteria from the stomal area of caecal urinary reservoir could inhibit bacteria isolated from the urine and vice versa. Antibiosis thus seems to be a possible ecologic mechanism in regulating bacterial colonization and subsequent infection. However, antibiosis could be demonstrated only with species occasionally isolated from the urine, e.g. *Acinetobacter*, *Alkaligenes* and *Pseudomonas*, not in tests with established urinary tract pathogens of the family of Enterobacteriaceae (VII). Absence of antibiosis may be one mechanism that allows bacterial colonization of the caecal reservoir.

UTI in patients with urinary reservoir diversion seems to have a benign course. In the series here presented, 18 patients with caecal reservoir were followed up for a total of 740 months, and only one patient has had symptoms of UTI. That patient, however, had a stricture of one of the uretero-caecal

anastomoses, thus illustrating the danger of UTI *and* obstruction rather than the risk of bacteriuria per se. Similar experience was reported by other authors (Benckroun et al., 1982; Kock et al., 1982).

Bacteriuria is present in most patients with caecal urinary reservoir, most often occurring in pure culture. Although the composition of urine from such reservoirs is more favourable than that of normal urine for bacterial growth, no major difference in growth rate was found. Factors that may significantly add to host protection against bacterial colonization and subsequent infection, are the production of large amounts of immunoglobulins, especially sIgA, and of mucin by the caecal mucosa, which exhibits preserved morphology. Antibiosis may likewise influence colonization of the reservoir. UTI in these patients seldom gives rise to symptoms.

Conclusions

Permanent urinary diversion today usually denotes an ileal or a colonic conduit. Considerable experience of these methods has been gained and the postoperative morbidity is not unacceptable. Conduit diversion undoubtedly remains the most suitable method for most patients, and is accordingly to be recommended. Its drawbacks, however, have become increasingly clear. Deterioration of renal function in the long-term view merits concern. In addition, there is a wide range of problems connected with the wet urostomy as such and the collection and storage of urine in an appliance attached to the body surface. These problems may cause psychosocial complications and adversely influence the patient's lifestyle.

During the past decade, alternative methods for urinary diversion have increasingly attracted interest. Appliance-free urinary diversion has been the aim of these methods. An important stimulus in the developmental efforts has been the favourable results obtained with the continent ileostomy in proctocolectomized patients, as evolved by Kock in Gothenburg. Continent urinary diversion has been attempted with ileal and with caecal reservoir.

Experience gained from clinical use of continent caecal reservoir, and results from the special investigations undertaken in these patients, permit the following conclusions.

1. Construction was more time-consuming for caecal reservoir than for conduit in urinary diversion and a higher postoperative complication rate might be inherent to this method.
2. The exclusion of the ileocaecal segment from the gastrointestinal tract should cause no disturbances of metabolism nor, if renal function is normal, of electrolyte imbalance.
3. The caecal reservoir provided adequate capacity for convenient emptying intervals. Intermittent high-pressure waves occurred within the full reservoir. The amplitude of these waves diminished with the passage of time, indicating increasing functional capacity.
4. Malfunction of the continence-providing ileal nipple valve was the most common complication. Revisional procedures were required in most patients before continence and ease in catheterization were achieved.
5. A full caecal reservoir could cause functional obstruction to urine flow.
6. The occurrence of strictures of 3 out of 36 uretero-caecal anastomoses might reflect the risk of using an unnecessarily elaborate technique to achieve reflux protection.
7. Renal function was well preserved at follow-up of these patients and compared favourably with the renal function in conduit diversion. Significant diminution of renal function was associated with caecal reservoir diversion only when stricture of the uretero-caecal anastomosis had occurred.

8. Most patients with caecal urinary reservoir had intermittent or persistent bacteriuria. Bacteria of the family of Enterobacteriaceae were found in cases with persistent infection. However, symptoms of urinary tract infection were rare.
9. Caecal reservoir urine differed from urine of individuals with intact urinary tract in a higher and more stable pH, a higher level of albumin, lower level of urea and higher 24-hour urine output. However, no major difference in bacterial growth between reservoir urine and normal urine was found.
10. The high amount of immunoglobulins, e.g. sIgA, and of mucin in urine from patients with continent caecal reservoir might constitute important host defence mechanisms against urinary tract infection. Microbial antibiosis might also be of importance to hinder reservoir colonization.

The continent caecal reservoir merits status as an alternative for urinary diversion, which might be preferable in selected patients. The attainable qualities of appliance-free stoma with intact peristomal skin and no odour are important and make the reservoir aesthetically superior to conduit diversion. The prospective gain in "quality of life" warrants further clinical trials of the continent caecal reservoir.

Acknowledgements

The friendly and stimulating atmosphere at the Department of Urology, University Hospital of Lund, has constituted an important basis for this work in clinical research. The work, however, could be realized only through fruitful cooperation with other departments.

I am most grateful to all who have been involved in the care and the study of the patients with continent caecal urinary reservoir. In particular, I would like to express my warm thanks to:

Professor Torsten Sundin for analytic and constructive penetration of scientific issues, his interest and constant encouragement.

Associate Professor Stig Colleen, friend and appreciated teacher in clinical and scientific matters, for his excellent guidance and whole-hearted support throughout the study.

Associate Professor Thomas White for his enthusiasm and never failing patience and for introducing me to the scintillation camera.

Professor Per-Anders Mårdh and *Associate Professor Arne Lundblad* for placing laboratory facilities at my disposal and for stimulating discussions.

Mrs Karin Löw for knowledgeable and highly valued help with the immunoassays.

Associate Professor Lillemor Forsberg, *Dr Hans Hedlund*, *Hospital Physicist Ingemar Larsson*, *Doctor of Science Kjell Lindström* and *Dr Anders Mattiasson* for pleasurable collaboration.

Associate Professor Per Alm and *Dr. László V. Soltész* for advice.

Mrs Ingrid Dahlman and *Miss Maj-Britt Jönsson*, head nurses of our urological wards, for patient care at its best.

Mrs Gertrud Hellmer, *Mrs Britt Mundt-Petersen* and *Miss Eva Sandgren* for excellent technical assistance.

Mr Michael Hartmann for advice on statistical matter.

Mrs Christina Parknäs and *Miss Ann-Christin Persson* for skilful secretarial help.

Mrs Ray McVeigh Källqvist for expert linguistic treatment of the English text.

Mr Jan Strömblad for talented artistry.

This study was supported by grants from the World Health Organisation, the Swedish Medical Research Council, the University of Lund and from the Maud and Birger Gustavsson Fund, Stockholm.

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Papers I—VII

I

Continent Caecal Reservoir in Urinary Diversion

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Summary

Construction of a continent urinary reservoir was attempted in 18 patients with carcinoma of the bladder. The caecum was used as reservoir and an intussuscepted ileal nipple was created to provide continence. 15 patients are alive and have been observed for 7 to 68 months. The most common complication was malfunction of the nipple valve with urinary leakage and/or difficulty in catheterization. Revision of the outlet was performed one or more times in eleven cases. The technique of nipple valve construction was successively evolved, with improvement in functional results. Stricture of one uretero-intestinal anastomosis occurred in three patients. Construction of a continent caecal reservoir is a complex procedure and the problem of a stable, continence-ensuring mechanism in the outlet has not been conclusively solved. The enhanced "quality of life" offered by a well manageable, continent reservoir nevertheless warrants continued clinical trials in selected patients.

Numerous methods have been devised for permanent supravescical diversion of urine, indicating that the ideal method has not yet been found. Despite revived interest in ureterosigmoidostomy in the past decade (Zincke & Segura, 1975; Marberger & Straub, 1982), diversion by means of ileal or colonic conduit is the method preferred by most urologists. Vast experience of conduit diversion has accumulated, and in most cases it is a safe procedure with acceptable results.

The initial enthusiasm for conduit diversion has become somewhat subdued, however. The reasons include deterioration of the renal function with time (Pitts & Muecke, 1979; Orr *et al.*, 1981), the wide range of problems inherent in the stoma as such and the constant wearing of an external appliance (Jeter & Lattimer, 1974; Dunn *et al.*, 1979; Jones *et al.*, 1980).

To obviate stoma complications and obtain appliance-free urinary diversion, attempts have been made to construct a continent intraabdominal reservoir. Ileum (Norlén *et al.*, 1975; Leisinger *et al.*, 1976; Madigan, 1976; Kock *et al.*, 1978; Kock *et al.*, 1982) and caecum (Ashken, 1974, 1982; Benckroun, 1977; Månsson & Sundin, 1977; Zingg & Tscholl, 1977) have been employed for this purpose. The present paper presents our experience with utilization of caecum as a continent urinary reservoir.

Patients and Methods

In the period 1977–1982, 18 patients underwent surgery for construction of a continent caecal bladder. The patient's age range was 38–68 (mean 53) years and all had high-grade invasive bladder carcinoma. In four cases the diversion

procedure and cystourethrectomy were performed in a single session and without preoperative radiotherapy. Staged procedure was used in the other 14 patients. The caecal reservoir was first constructed and 3 to 4 weeks later preoperative pelvic irradiation was begun. Four patients received 45 Gy during 4 weeks and 10 received 20 Gy during 5 days. The interval between radiotherapy and cystourethrectomy was 4 weeks in the first group of patients and a few days in the second group.

Surgical procedure

The abdomen was opened through a low midline incision. The ureters were dissected and transected close to the bladder. The ileum was divided 20 cm from the ileocaecal sphincter and the ascending colon was divided 12–15 cm from this sphincter. Bowel continuity was restored by end-to-end ileocolic anastomosis. The appendix was removed. To facilitate inspection of the ileocaecal sphincter, the caecum was opened along a taenia.

In the ureterocaecal anastomosis two anti-reflux techniques were combined, viz. a submucosal tunnel 3–4 cm long, made from within the caecal cavity (Goodwin et al., 1953) and a split-cuff ureteral nipple (Turner-Warwick & Ashken, 1967). Sutures were made with 4/0 chromic catgut. The anastomosis was splinted with a baby-feeding catheter, 8 F or 5 F.

The continence-providing principle was an intussuscepted ileal valve. As experience was gained the technique was modified to enhance stability of the nipple valve.

Intussusception of ileal valve into caecum – group A, 5 patients (Fig. 1). The peritoneum covering the mesentery of the distal 10 cm of ileum was removed.



Fig. 1. Intussuscepted ileal nipple valve protruding into the caecum.

Multiple seromuscular incisions were made with electrocautery in the ileal wall, in order to produce a raw surface which would promote adhesion between the two bowel layers of the valve. During creation of the valve, the intestine was rotated 180° in order to avoid bulking of mesentery (Kock *et al.*, 1977). The mesentery was slit at the future tip of the nipple. A 2/0 seromuscular silk suture was inserted at one side of the ileum close to the ileocaecal sphincter, taken through the mesenteric slit and fixed to the opposite wall proximal to the slit and at an equal distance from it. When this suture was tightened, and the ileum simultaneously was manually intussuscepted, the two walls of the nipple rotated. Two rows of 3/0 seromuscular silk sutures were placed circumferentially between the walls of the nipple, at its base, reaching as close to the margins of the mesentery as possible. A 5 cm long nipple then protruded into caecal cavity (Fig. 1).

Intussusception of ileal nipple valve within the ileum – group B, 7 patients (Fig. 2). Instead of protruding into the caecum, a nipple valve 5 cm in length was positioned within the ileum, just proximal to the ileocaecal sphincter. To diminish the bulk of mesentery between the nipple walls, as much fat as possible was carefully removed from between the mesenteric blood vessels. A Babcock clamp was inserted through the ileocaecal sphincter, grasping the ileal wall at the site preselected for the nipple tip. By slow retraction of the clamp, an ileo-ileal intussusception was achieved. During this manoeuvre, 3/0 seromuscular silk sutures were placed step by step between the nipple walls.

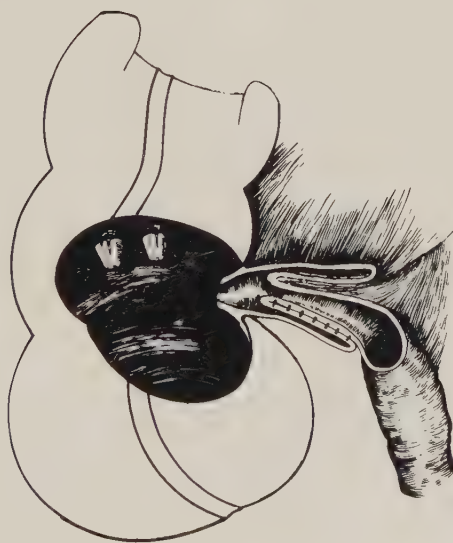


Fig. 2. Intussuscepted ileal nipple valve within the ileum.

Intussusception of ileal nipple valve within the ileum and mesenteric exclusion – group C, 6 patients (Fig. 3). In addition to the modification employed in group B, the mesentery was completely stripped from the ileum for a distance of 6–7 cm, corresponding to the midportion of the segment to be used in construction of the nipple valve.

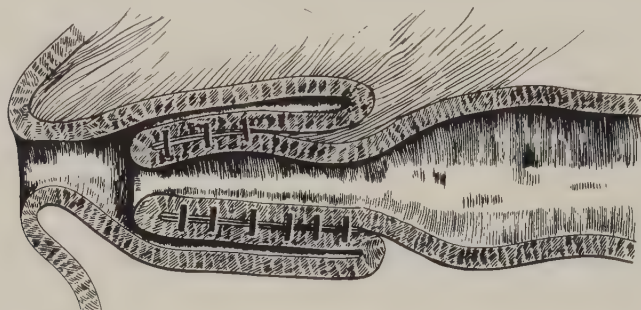


Fig. 3. Intussuscepted ileal nipple valve with mesenterial exclusion.

In all patient groups the reservoir was drained with a 24 F (Medena®, Astra-Meditec, Mölndal, Sweden) or a Foley-type silicone catheter which, together with the baby-feeding catheters, was brought out through the nipple valve. The caecum was closed in two layers, using absorbable sutures. The patency of the suture line and of the nipple valve was tested by inflating the reservoir with air.

The ileum was brought out through the rectus muscle below and to the right of the umbilicus. The base of the nipple valve was anchored with 3/0 silk sutures to the abdominal wall. Redundant ileum was excised and a stoma was fashioned flush with the skin.

Doxycycline was administered during the operation and for four days thereafter. The baby-feeding catheters were removed after ten days and the reservoir-draining catheter after three weeks. During these weeks the reservoir was irrigated daily with normal saline solution to remove mucus. The patients were then instructed in the technique of clean but not sterile self-catheterization. They emptied the reservoir at two-hourly intervals for the first two days, and then at progressively longer intervals, using one of the previously mentioned catheters.

Results

Postoperative complications required surgery in three patients, viz. bowel obstruction and insufficiency of the intestino-intestinal anastomosis, urine leakage, probably from the caecal suture line, and impaired circulation to the stoma due to compression of the mesentery. Postoperative recovery was uneventful in the other 15 patients.

Complications during follow-up

Reservoir outlet. Revision of malfunctioning nipple valve to ensure continence and/or facilitate catheterization was a common requirement (Table 1). More than one revision was done in some patients.

Table 1. Results of urinary diversion with continent caecal reservoir, using three modifications of reservoir outlet.

<i>Group (definitions, see text)</i>	<i>No of patients</i>	<i>Revision of malfunctioning reservoir outlet</i>	<i>Continence achieved</i>	<i>Reservoir stone</i>	<i>Stricture of ureterocaecal anastomosis</i>	<i>Deaths</i>
A	5	4	3	1	2	1
B	7	4	5	2	1	1
C	6	3	5	—	—	1

All the *group A* patients experienced urinary leakage and catheterization difficulties within a few months. Exploration showed the cause to be sliding of the nipple valve. The valve thus was short, usually completely extinguished at the mesenteric border.

In one *group B* patient there was severe incontinence immediately following postoperative removal of the catheter drain. At exploration the nipple valve was seen to be symmetric and without sign of sliding. Attempts to refashion the nipple were unsuccessful, and it was removed. The caecum has since functioned as conduit in this patient. Revision in two other *group B* patients showed sliding of the nipple valve, combined in one case with a large pouch of ileum between the abdominal wall and the base of the valve. In a patient who found catheterization difficult, the nipple valve per se was not malfunctioning, but the distance between the ileocaecal sphincter and the tip of the valve was so long that the catheter was caught in a pouch between these structures. The sphincter was opened up widely and thereafter this problem was resolved.

No patient in *group C* has had leakage of urine. The main problem in this group has been catheterization difficulties. Exploration in three cases showed incomplete adherence of the nipple base to the abdominal wall, with formation of a large ileal pouch between these structures. The nipple valves were symmetric, without sliding tendency. All of them, however, showed signs of deficient blood supply at the tip – yellowish-brown pallor and thickening of the wall with relative stenosis.

Reservoir. Calculi were detected in the reservoir in three patients. The stones were removed by endoscopic litholapaxy or at the time of nipple valve revision.

Ureterocaecal anastomoses. Stricture of one ureterocaecal anastomosis arose in three patients within 12 months after the urinary diversion. Reimplantation of the ureter into the reservoir without reflux protection was done in two of these patients, with restoration of normal kidney function in one of them, but not in the other. Non-functioning kidney and pyelonephritis necessitated nephrectomy in the third patient.

Functional follow-up

Survival. In July 1983, 15 of the 18 patients were alive after observation periods of 7 to 68 months (mean 39 months). Two of the three deaths occurred from metastatic disease 12 and 15 months, respectively, after urinary diversion. In

one of these patients (group A), urinary leakage and catheterization difficulty began shortly after the diversion operation. No revision of the nipple valve was attempted, the reservoir being drained via a catheter until death. In the second patient (group B) the reservoir functioned well and at autopsy a symmetrical, 5 cm long valve was found. The third death occurred from complications after the cystourethrectomy, performed in a second session.

Nipple valve function. Of the 15 surviving patients, three wear collecting appliances because of leakage from the valve. In one of the three the leakage is minimal and infrequent, but the patient feels more secure with the bag. He empties the reservoir through a small opening in the bag. In the second patient the caecum functions as conduit. The third patient remains incontinent despite two attempts to reconstruct the nipple valve. The other 12 patients are continent and empty their reservoirs at intervals of three to five hours. The stoma is covered with gauze pad or Hollister Stoma Cap® (Abbott). Some difficulty is occasionally experienced in catheterization by two patients, especially at high volume in the reservoir. A tendency to prolapse of the nipple valve necessitates use of a small stoma-covering truss in three cases (1 group A, 2 group B).

Renal function. The patients have been regularly re-examined with urography, ⁵¹Cr-EDTA clearance and scintillation camera renography. Urography has shown normal upper urinary tracts with minimal or no dilatation (Fig. 4), except in the patients with stricture of ureterointestinal anastomosis. In two of these patients, the radionuclide studies showed loss of renal function. In the other patients, renal function was unchanged at follow-up.



Fig. 4. Intravenous urography in a 53-year-old man 4 years after urinary diversion with use of a continent caecal urinary reservoir.

Reflux. Nine patients were examined concerning reflux from the reservoir to the upper urinary tract and residual urine in the reservoir. This investigation was done 3 to 36 (mean 19) months after the diversion procedure. The reservoir was filled with 200–400 (mean 320) ml of iodine-containing contrast

medium and exposures were made immediately and after 30–45 minutes. Catheterization was then performed and another film was taken. No reflux was found, except in the two patients with reimplantation of one ureter into the caecal reservoir. Reflux to the renal pelvis was seen in these patients, but only minimal dilatation of the upper urinary tract. The reservoirs were shown to be completely emptied (Fig. 5 a, b).

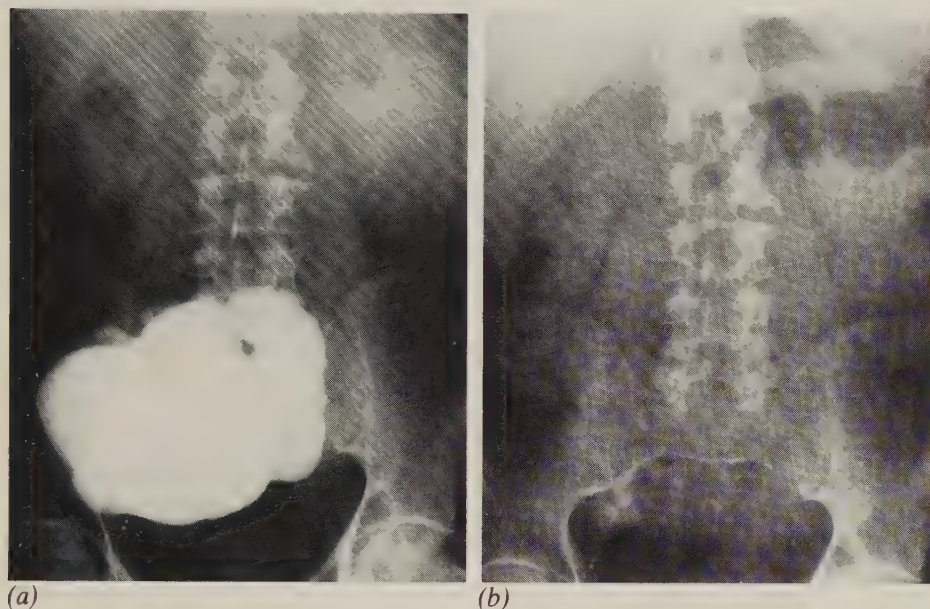


Fig. 5. Reservoirography in a 63-year-old man 3 years after construction of a caecal urinary reservoir. Exposure 45 min after instillation of 400 ml contrast medium (a) and after emptying of the reservoir (b).

Urinary microbiology

Most of the patients did not receive prophylactic antibiotic treatment. Urine cultures often showed growth of Gram-negative aerobic microorganisms. In the few patients who received trimethoprim 100 mg daily since the urinary diversion, the cultures were usually negative. Clinical signs of urinary tract infection were seen in only one patient, whose urogram showed a non-functioning kidney due to stricture of the uretero-intestinal anastomosis.

Metabolism

Except for occasionally slightly lowered base excess, acid-base balance and serum electrolytes were normal in all the patients throughout the observation period. Liver function tests have remained normal. Diminution of serum cobalamin occurred two years after urinary diversion in one case and was treated with vitamin B₁₂. This was the patient in whom bowel obstruction and insufficiency of the intestino-intestinal anastomosis appeared soon after urinary diversion, necessitating resection of small and large bowel. Serum cobalamin and folic acid levels have been normal in the other patients.

Social readjustment

Ten of the 15 surviving patients were able to resume their former occupations. Two were sick-listed until normal retirement age and three were still on sick leave at the end of the study period.

Adaptation to self-catheterization was swift. When the patients had experienced appliance-free living, temporary need of a collecting appliance because of urinary leakage was experienced as negative. The patients do not experience restrictions in their vocational or social life, though they have found occasional difficulties in catheterization to be disconcerting.

Discussion

The choice of method for urinary diversion poses formidable problems in individual cases. Basic factors in the decision are the urologist's preferences, the patient's age, physique and mental status, the underlying disease and the aesthetic requirements. The aesthetic aspects mirror the individual patient's total concept of himself in relation to society.

The emotional implications of a wet stoma and the presence of a collecting appliance can seriously restrict the patient's life following urinary diversion (Dunn *et al.*, 1979; Jones *et al.*, 1980). Although most patients seem to adjust to ostomy, it undeniably influences perception of the personal "body image" (McCawley *et al.*, 1975).

Interest in appliance-free urinary diversion was greatly stimulated by reports from Kock and co-workers in Gothenburg, Sweden, on construction of a continent ileal reservoir for proctocolectomized patients. Kock (1971) used the intussuscepted ileal valve described by Perl (1949) as continence-providing principle.

An ileal reservoir constructed for urinary diversion gave encouraging results in relatively small series of patients (Leisinger *et al.*, 1976; Madigan, 1976; Kock *et al.*, 1982). This rather complicated method involves splitting and folding of an ileal segment in a special way and construction of two intussuscepted ileal nipple valves – an afferent to prevent reflux and an efferent to achieve continence. The main complication has been malfunction of the nipple valves due to sliding, with reflux and leakage of urine, respectively, necessitating surgical revision.

The caecum has a much longer history of use as a urinary reservoir (Verhoogen, 1908; Makkas, 1910), with the appendix as outlet. The caecal reservoir attracted renewed interest in the 1950s, when the distal ileum was used as outlet, with reliance on the ileocaecal sphincter and peristalsis of the ileal segment towards the caecum for provision of continence (Gilchrist *et al.*, 1950; Merricks & Gilchrist, 1957; Sullivan *et al.*, 1973). Other authors, however, confirmed the opinion expressed by Verhoogen as early as 1908 that continence was not achievable with this method (Bricker, 1950; Harper *et al.*, 1954; Brendler, 1974). The absence of reports on the method in the past ten years testifies to its unreliability concerning continence.

An intussuscepted ileal nipple valve protruding into the caecal cavity was hoped to provide continence (Månsson & Sundin, 1977; Zingg & Tscholl, 1977). Within a few months, however, all of our patients experienced urinary leakage and difficulty in inserting the catheter. Surgical exploration showed the nipple valve to be extinguished or very short.

In these patients (group A) we used the technique described by Kock *et al.* (1977), with 180° rotation of the ileum to flatten out and separate the mesentery to the inner and outer walls of the nipple valve. Positioning of the stabilizing sutures between the nipple walls is difficult with this technique, however. Sliding of the nipple valve is probably due to the dynamics within the reservoir in which intermittent high-pressure waves occur at fullness or near fullness. Amplitudes of 30–50 cm H₂O are frequent (Hedlund *et al.*, 1984). This high pressure can directly affect the intraluminal surface of the nipple valve, tending to evaginate the nipple. Concomitantly, the high tensions in the reservoir wall that generate the pressure waves may act on the nipple base, tending to tear the nipple walls apart. Similar experience with an intracaecal ileal nipple valve was reported by Zingg (1978).

We first modified the method by positioning the nipple valve within the ileum, thus leaving an intact ileocaecal sphincter between the reservoir and the valve. This sphincter has been shown to possess features of a true alimentary tract sphincter in humans, with intraluminal pressure exceeding that of its adjacent cavities. The sphincter relaxes with balloon distension of the terminal ileum just proximal to it and contracts with caecal distension (Cohen *et al.*, 1968). Preservation of the sphincter might, we thought, diminish the effect of the reservoir dynamics on the nipple valve. The positional change in the nipple valve was combined with removal of mesenteric fat to decrease the bulk of mesentery between the nipple walls. Although the results as regards continence were improved, these valves were incompetent in some patients, and there were also difficulties in catheterization or prolapse of the nipple valve.

A further step to improve stability of the nipple valve was to strip the mesentery from the ileum for a distance of 6 to 7 cm (Hendren, 1980). Circumferential seromuscular sutures could then be placed between the nipple walls. Only part of the nipple valve thus had intervening mesentery (Fig. 3). This technique (group C) gave stable nipple valves, and all five surviving patients have been continent during observation periods of 6 to 12 months. In three of them, however, reoperation was necessary because of difficulties in passing the catheter. The fault was not in the nipple valve as such, but inadequate fixation of the nipple base to the abdominal wall had caused angulation. Repeated pushing with the catheter dilates this part of the ileum, eventually creating a pouch. To ensure a straight outlet, a strip of fascia or Marlex® mesh, placed around the base of the nipple valve, passing through the mesentery to the nipple base and sutured to the posterior rectus sheath was suggested by Kock *et al.* (1980).

A possible danger arising from mesenterial exclusion is inadequacy of the blood supply. Such inadequacy was obvious from findings at revisional surgery in our patients; the nipple tip being yellowish-brown, fibrotic and relatively stenotic. The seromuscular incisions with cautery to scarify the walls of the nipple valves probably were contributory in this respect. We presently exclude only 5 cm of mesentery and cauterize the nipple wall. These measures, together with seromuscular silk sutures, were the most satisfactory combination for nipple valve stability in experiments on dogs (Cranley & McKelvey, 1981). Use of a stapling instrument as advocated by Steichen (1977) did not improve stability of the nipple valve in these experiments, although it shortened the operating time.

As the pressure within the reservoir intermittently reaches high levels and the reservoir urine often contains bacteria, a reflux-proof ureterocaecal anastomosis is obviously necessary. The technique we used for this purpose was rather intricate, and stricture arose in 3 of the 36 anastomoses. We attributed

these strictures to necrosis of the ureteric nipples which were not detectable at surgical correction. The strictures, moreover, were short.

Although two patients had free reflux of infected urine after ureteric reimplantation and relatively high pressure in the reservoirs, no detrimental effect on the upper urinary tract has been observed so far. The high excretion of immunoglobulins, especially secretory IgA, from the caecal reservoir may contribute to protect the kidney against bacterial infection (Månsson *et al.*, 1984).

Other methods have been described for construction of a continent caecal urinary reservoir. An ileocaecal segment was isolated and the ureters were implanted with antireflux technique in the distal part of the ileum (Ashken 1974, 1978, 1982). In his last modification the continence-providing principle was a "flutter valve", constructed from a separate ileal isolate, that was sutured into the open end of the caecum. At least 5 cm of the ileum hung into the caecum, but with its antimesenteric border attached to the lateral caecal wall. Complications were urinary fistula where the ileal mesentery passed into the caecum and sliding of the valve. The flutter valve showed a tendency to spontaneous eversion of the tip, i.e. conversion to a spout valve.

An ileocaecal segment was employed also by Benckroun (1977, 1982) who anastomosed the ureters end-to-side to the distal ileum and relied on the ileocaecal sphincter to protect against reflux. A separate ileal isolate was folded inwards, giving an "inkwell" valve, which was attached to the open end of the caecum. The other end, with serosal covering and mesentery, constituted the stoma. Continence was claimed to have been achieved in 24 of 27 patients. The main complication was prolapse of the valve, but no damage was caused to the exposed mesentery by catheterization (Benckroun, 1982, personal communication). Reflux to the upper urinary tract occurred in many patients at a reservoir volume of 300 to 350 ml.

The dry stoma of a continent reservoir is unquestionably superior to the wet stoma of a urinary conduit, with its constant need of a collecting appliance. Despite considerable progress in quality of appliances and in ease of management, a plastic bag attached to the body with risk of leakage, peristomal skin irritation and offensive odour may restrict the patient's lifestyle and be emotionally disturbing. For some patients, therefore, a reservoir may be preferable to conduit diversion of urine, provided that complete continence and ease of catheterization can be achieved.

The main problem in construction of all reservoirs, whether for intestinal contents or for urine, is the provision of a continence-ensuring outlet. In evolving a reliable mechanism for this purpose, animal experiments have been of little benefit, and most experience has been gained through trial and error in humans. The high complication rate during the early period of development, with incontinence and catheterization difficulties, has successively been reduced (Kock *et al.*, 1980; Ashken, 1982). Our study also illustrates this progress. Selection of patients is important because of the complexity of the surgery required and the risk that the nipple valve may have to be refashioned. The technically simpler and less time-consuming conduit diversion remains the method of choice for most patients who are to undergo radical surgery for bladder cancer. The gain in quality of life with a continent urinary reservoir, however, warrants further clinical trials in centres with special interest in this field.

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Dynamics of a Continent Caecal Reservoir for Urinary Diversion

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Summary

Motor activity of the caecal reservoir for urine, and of the intussuscepted nipple valve in the ileal outlet, was studied in seven continent and two incontinent patients by means of a catheter equipped with two microtransducers. The basal pressure was low in the reservoir even at large-volume filling. In the continent patients the basal pressure was always higher in the ileal outlet than in the reservoir. No high-pressure zone was present in the outlet in the incontinent patients. Intermittent pressure waves occurred in the reservoir, and they increased in frequency, duration and amplitude with increasing filling. Pressure waves with higher amplitude arose simultaneously in the outlet. Increasing time from construction of the reservoir was accompanied by decreasing amplitude of the pressure waves, indicating adaptation towards larger functional capacity of the reservoir. The recorded dynamics seemed to reflect the functional state of the reservoir.

The possibility of urinary diversion by means of an appliance-free, continent reservoir has attracted renewed interest in the past decade. Ileum (Kock *et al.*, 1982) and colon (Ashken, 1974; Benckekroun, 1977; Zingg & Tscholl, 1977; Månsson *et al.*, 1984) have been used for this purpose. The intraluminal pressure in such reservoirs ideally should be low. But studies on ileal reservoirs for urine (Norlén & Trasti, 1978) and for intestinal contents after proctocolectomy (Akwari *et al.*, 1980) revealed that considerable intraluminal pressures may be reached when the reservoir is full. The tension in the reservoir wall that generates such pressures has been attributed responsibility for malfunction of ileum reservoir outlet (Norlén & Trasti, 1978). Such malfunction has been a frequent problem also when caecum is used as reservoir (Ashken, 1982; Månsson *et al.*, 1984).

The investigations here presented concerned the dynamics of the caecal urinary reservoir as regards pressure generated within the reservoir and within the continence-providing nipple valve at different filling volumes and different postoperative intervals. Attempts were made to correlate the findings with the functional state of the reservoirs.

Patients and Methods

Seven men with continent and two with incontinent caecal urinary reservoir were studied. Their age range was 39–63 years (mean 56). The urinary diversion had been performed in the treatment of high-grade invasive bladder carcinoma 3 to 49 (mean 17) months before the first of the investigations here

reported. An intussuscepted nipple valve in the reservoir outlet was responsible for continence. The valve had been constructed from the distal segment of ileum just proximal to the ileocaecal sphincter, which thus was left intact (Månsson *et al.*, 1984).

Two of the seven men in the continent group had to empty the reservoir at 3-hourly intervals to avoid leakage. Emptying intervals in the other five cases were four to five hours. The two incontinent men used a collecting appliance. One of them had been primarily continent, and he is included also in the first group. In the second patient the continence-providing nipple valve in the ileal outlet had to be removed because of leakage and difficulties in catheterization.

With the patients mildly dehydrated and in supine position, the following studies were performed in the *continent patients* after emptying of the reservoir.

1. Pressure recordings simultaneously in the reservoir and in the nipple valve during *continuous filling* of the reservoir with physiologic saline solution at 37°C via a baby-feeding catheter 8 F at a flow rate of 9 ml per minute, using a mechanical pump. Filling was continued until the patient experienced fullness or leakage occurred. Altogether 14 investigations were performed. Five of the seven patients were studied two or three times, with intervals of 6 to 37 months.

2. Recordings of nipple valve pressure profiles at *intermittent filling* of the reservoir in stepwise fashion, with increments of 100 ml. The infusion catheter was removed before pressure recording. Nine studies were performed in five patients.

In the *incontinent patients* pressure recordings were done only at small filling (< 100 ml) because of leakage.

Pressures in the reservoir and in the nipple valve were registered via a silicone 7 F catheter equipped with two distal microtransducers mounted 6 cm apart (series 16 CT, Gaeltec). Abdominal pressure was recorded as rectal pressure by means of a balloon catheter connected to a transducer (746, Siemens). Both systems were connected, for patient safety, to isolated pressure transducer amplifiers and a recorder (Linear corder mark III, Watanabe).

The accuracy of the pressure measurement system was controlled at regular time intervals. The static performance was calibrated against a variable fluid column and the dynamic properties of the catheter-manometer combination was verified using the step-response method. The rise-time of the system showed consistently to be around 120 msec. Electrical calibration of the transducers was performed before and after use. The measuring catheter with the two microtransducers was placed within the reservoir. This position was checked by identical response to a Valsalva manoeuvre. Positioning of the distal transducer in the reservoir and the proximal transducer in the nipple valve for the continuous filling studies was accomplished by retraction of the catheter. Accurate position of the catheter was assumed when the proximal transducer recorded a phasic activity or pressure waves with higher amplitude than in the reservoir.

For the pressure profile recordings at intermittent filling we used a mechanical catheter withdrawer with a speed of 2.5 mm/s (Siemens). At least three recordings were done at each volume.

Statistical calculations were done with use of the paired t-test.

Results

Continent patients

The basal pressure in the reservoir was low at near-emptiness, but rose with increasing filling. The data are presented in Table 1. The basal pressure was always somewhat higher in the nipple valve than in the reservoir (6 ± 1 cm H₂O, $p<0.001$). An intermittent phasic activity with a frequency of 7–10 c/min was recorded in the nipple valve in all patients. The amplitude of these waves varied from 5 to 25 cm H₂O (Fig. 1).

Table 1. Basal pressure in the caecal reservoir and in the ileal nipple valve at progressive filling of the reservoir (mean $\pm$ SEM). 14 investigations in 7 continent patients; n=no of fillings at given level; discrepancies between n in reservoir and nipple valve due to difficulties in accurate positioning of the transducer in the valve.

Basal pressure cm H ₂ O	Level of reservoir filling (ml)					
	0–99	100–199	200–299	300–399	400–499	500–599
Reservoir	n=12 11 $\pm$ 1	n=13 13 $\pm$ 1	n=13 15 $\pm$ 1	n=11 15 $\pm$ 1	n=6 16 $\pm$ 1	n=3 19 $\pm$ 3
Nipple valve	n=8 18 $\pm$ 2	n=8 21 $\pm$ 2	n=9 22 $\pm$ 2	n=7 23 $\pm$ 2	n=3 26 $\pm$ 4	n=2 26 $\pm$ 5

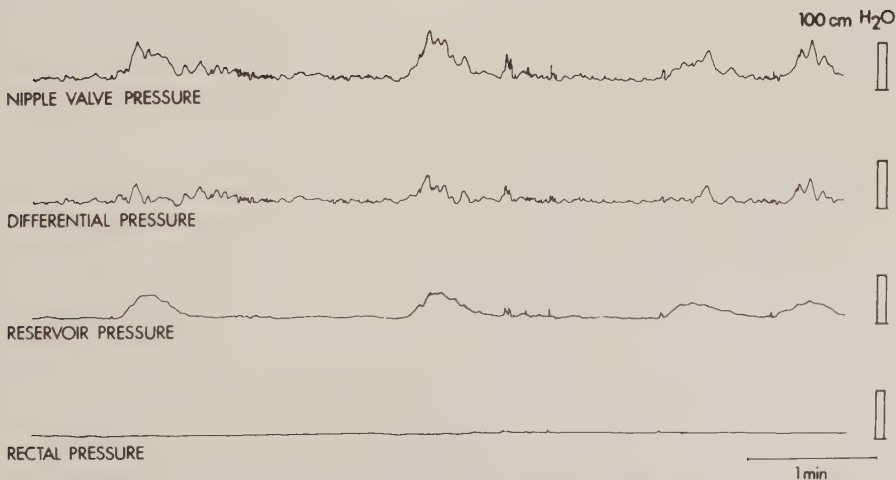


Fig. 1. Pressures recorded from a caecal urinary reservoir, ileal outlet and rectum in a 50-year-old man, 12 months after urinary diversion. Reservoir volume at start of registration 420 ml.

Table 2. Functional length and maximum amplitude of the nipple valve pressure profile at different reservoir volumes (mean $\pm$ SEM). 9 investigations in 5 continent patients; n=no of studied profiles.

	Reservoir volume (ml)				
	100	200	300	400	500
Functional length (mm)	n=21 21 $\pm$ 1	n=21 19 $\pm$ 1	n=28 22 $\pm$ 1	n=9 22 $\pm$ 2	n=9 19 $\pm$ 2
Maximum amplitude (cm H ₂ O)	n=21 21 $\pm$ 3	n=21 27 $\pm$ 3	n=28 24 $\pm$ 2	n=9 21 $\pm$ 2	n=9 26 $\pm$ 5

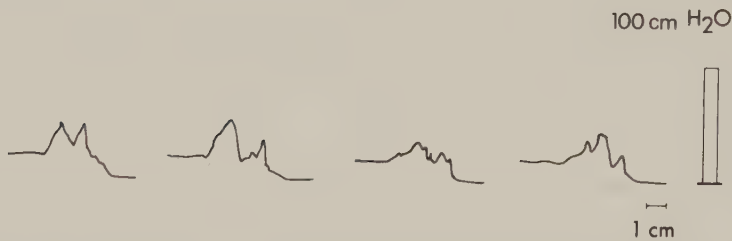


Fig. 2. Pressure profiles from the ileal nipple valve in a 50-year-old man, 12 months after urinary diversion to a caecal reservoir. Reservoir volume 400 ml.

The nipple valve pressure profiles showed that the functional nipple length, defined as the extent of the nipple along which the nipple pressure exceeded the intrareservoir pressure, was around 20 mm (Table 2). In the individual patients, however, the functional nipple length varied from one profile recording to another (Fig. 2). No correlation was found between degree of reservoir distension and functional nipple length. The peak of the profile pressure was most often below 30 cm H₂O and showed intraindividual variations. It did not increase in response to filling. Between the two patients with risk of leakage at high filling and the other patients there was no discernible difference in amplitude of pressure or length of the nipple pressure profile.

Intermittent pressure waves as an expression of caecal reservoir contractions were recorded in the reservoir (Table 3). At filling volumes of 200–500 ml, pressure waves were seen every second to third minute. Their appearance was either isolated, in regular or irregular fashion, or in clusters of two to five waves. In the individual patients the pattern of pressure waves did not change from one examination to another. Coughing or straining could often elicit pressure waves. Comparisons of pressure waves recorded at low and high reservoir filling in individual patients showed that frequency, duration and amplitude all increased significantly with increasing filling (frequency $p<0.001$, duration $p<0.01$, amplitude $p<0.05$).

The intrareservoir pressure waves were always accompanied by pressure waves in the nipple valve (Fig. 1). The valve waves were of considerably greater amplitude than the reservoir waves ($p<0.01$ at filling <500 ml). Initiation of the waves was always simultaneous in the reservoir and in the nipple

Table 3. Frequency, duration and maximum amplitude of pressure waves in the caecal reservoir and maximum amplitude of pressure waves in the ileal nipple valve at progressive filling of the reservoir (mean $\pm$ SEM), 14 investigations in 7 continent patients. n=no of fillings at given level (frequency calculations) or no of pressure waves (duration and amplitude data).

	<i>Level of reservoir filling (ml)</i>					
	0–99	100–199	200–299	300–399	400–499	500–599
Frequency (c/min)	n=13 0,05 $\pm$ 0,03	n=14 0,15 $\pm$ 0,02	n=13 0,30 $\pm$ 0,04	n=11 0,36 $\pm$ 0,05	n=5 0,45 $\pm$ 0,07	n=3 0,41 $\pm$ 0,06
Duration (sec)	n=6 43 $\pm$ 3	n=27 40 $\pm$ 2	n=50 45 $\pm$ 1	n=46 45 $\pm$ 2	n=26 49 $\pm$ 2	n=7 57 $\pm$ 4
Maximum amplitude (cm H ₂ O)						
in reservoir	n=6 55 $\pm$ 8	n=27 56 $\pm$ 4	n=50 47 $\pm$ 3	n=46 48 $\pm$ 3	n=26 41 $\pm$ 3	n=7 53 $\pm$ 10
in nipple valve	n=6 108 $\pm$ 13	n=19 149 $\pm$ 18	n=33 105 $\pm$ 12	n=24 106 $\pm$ 13	n=7 92 $\pm$ 6	n=3 71 $\pm$ 8

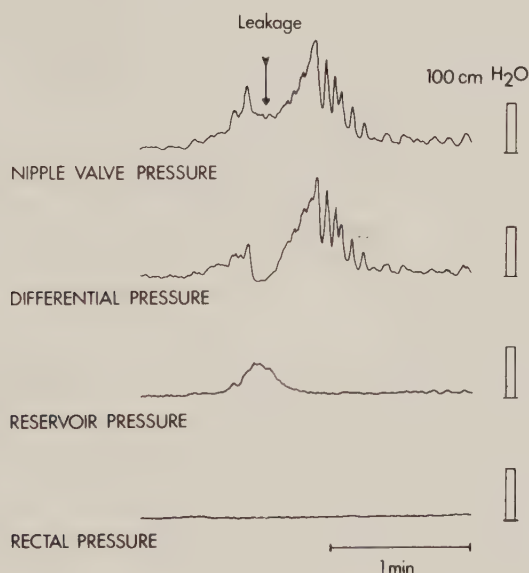


Fig. 3. Pressures recorded from a caecal urinary reservoir, ileal outlet and rectum in a 62-year-old man, 52 months after urinary diversion. Leakage occurred at 400 ml.

valve. Peaking of the pressure waves was likewise simultaneous in most recordings, but delay to the peak of nipple valve pressure was found in four patients. The delay occurred only on one and two occasions, respectively, in two patients and amounted then to 5–10 seconds. In the two other patients, who sometimes experienced leakage at high filling, longer delays were observed. In one of them there were delays of 13–35 seconds to the peak of most nipple valve pressure waves, associated with small leakages (Fig. 3). In the other

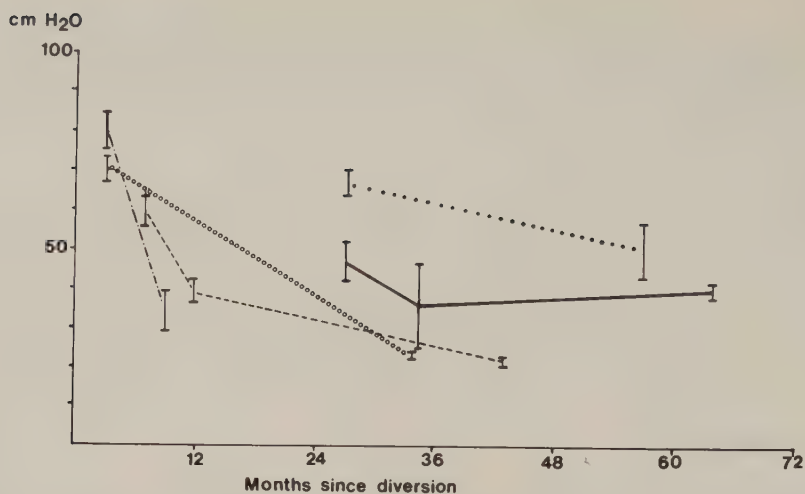


Fig. 4. Changes in maximum amplitude of pressure waves in caecal reservoir with time after reservoir construction. Identical fillings levels used for the comparisons (means $\pm$ SEM) in five continent patients.

patient the delays were 6–24 seconds. Subsequent exploration of the ileal outlet in the first of these two patients revealed sliding of the nipple valve.

The duration of the pressure waves was usually identical in the reservoir and in the nipple valve. Delay in reaching the peak of nipple valve pressure, however, was always associated with longer duration of the wave.

In the five patients who were investigated more than once, the amplitude of the pressure waves in the reservoir diminished ($p < 0.01$) as time from creation of the reservoir increased (Fig. 4). Frequency or duration of the waves showed no such change.

Incontinent patients

No reservoir function was preserved in these two patients. Leakage occurred at filling less than 100 ml. The basal pressure in the reservoir was 11 and 14 cm H₂O, respectively, when continuous leakage occurred. In the ileal outlet the basal pressure was the same or lower (0–5 cm H₂O). As in the continent patients, phasic activity was found in the outlet. Recordings of the pressure profile in the outlet revealed no zone of high pressure.

Discussion

A prerequisite for the continence of a reservoir is that the intraluminal pressure is always higher in the outlet than in the reservoir. The present study showed low intraluminal basal pressure in the caecal urinary reservoir during most of the time required for filling, in agreement with previous findings (Ashken, 1982). Leakage was then prevented in the continent patients by the somewhat higher pressure within the outlet. Contrastingly, a negative closure pressure was found in the incontinent patients.

Studies of intact small bowel have shown that the basic motility is segmental contractions. In the terminal ileum these contractions occur at a rate of about 8 per minute. This activity is reflected with the same frequency in electromyo-

graphic recordings (Duthie, 1979 a). Our pressure recordings in the reservoir outlet showed phasic activity most of the time, with frequency 7 to 10 c/min, also in patients with incontinent reservoir. The patients were unaware of this activity. Similar activity has been recorded in ileal conduits (Scherstén, 1962) and in nipple valves of ileal reservoirs in proctocolectomized patients (Nordgren *et al.*, 1982). Myoelectric studies showed the same frequency in the ileal reservoir when empty as when distended (Akwari *et al.*, 1980). Normal electromyographic and motor activity thus seems to be retained in excluded parts of ileum used as conduit, reservoir or outlet from a caecal reservoir.

The nipple valve pressure profiles recorded at different reservoir volumes showed variability in functional length and in amplitude in individual patients with continent reservoir. The basal pressure in the nipple valve probably accounted for most of the amplitude of the pressure profile, and the spontaneous activity in the three layers of bowel surrounding the lumen of the intussuscepted valve may have been responsible for the amplitude variation. Spontaneous activity was present also in incontinent patients.

In this study there was a relationship between the pressure profile in the ileal outlet and the functional state of the reservoir. Thus, no positive closure pressure was found in incontinent reservoirs. Some contradictory observations were published from a study on proctocolectomized patients with ileal pouch diversion (Myrvold & Johnsson, 1979). These authors found a high-pressure zone in incontinent patients with or without a nipple valve in the outlet. The pressure was higher in the continent patients, however.

Studies of intact right colon showed considerable variations in motor activity (Kock *et al.*, 1968). Retrograde peristalsis seems to occur and progression of colonic contents is slow (Duthie, 1979 b). We found that high intraluminal pressure waves occurred with increasing frequency as filling of the caecal urinary reservoir progressed. The patients experienced these pressure waves as episodes of slight cramp-like sensation at high-volume filling. In the patients' daily routines such sensations were an indication for emptying of the reservoir. Although the frequency and duration of the pressure waves did not change, the amplitude of the waves diminished with passage of time from construction of the reservoir, probably expressing increased volume capacity of the reservoir.

In the first urinary caecal reservoirs we constructed, the ileal nipple valve was fashioned to protrude into the caecal cavity through the ileocaecal sphincter, which thus constituted the nipple base. Difficulties in catheterization and leakage of urine soon appeared in these cases (Månsson *et al.*, 1984). The cause appeared to be forceful separation of the nipple valve structures due to high tension of the bowel wall layers at the nipple base. An intact ileocaecal sphincter, with the nipple valve inside the ileum, was judged to lessen this negative influence of tension on the valve. With this modification, the functional results improved. This might also have been due to improved technique leading to stabilization of the nipple valve, however.

In the present investigation, the pressure waves in the outlet were initiated simultaneously with those in the reservoir, indicating a direct effect of the intrareservoir pressure on the valve. Similar observations were made by Nordgren *et al.* (1982), in patients with an ileal reservoir for intestinal contents. In our study the pressure waves were always higher in the outlet than in the reservoir and sometimes reached considerable amplitudes. This may have been an effect of the tension in the bowel layers constituting the nipple walls. If this tension is regarded as identical to that in the reservoir wall, higher pressure will be generated in the nipple valve than in the reservoir, because of the smaller radius of the valve (Laplace's law).

Some observations on the human ileocaecal junction zone (Cohen *et al.*, 1968) may be relevant in the present context. These authors found at the ileocaecal junction a 4 cm long zone with intraluminal pressure higher than in the colon. The pressure in the junctional zone rose when the colon was distended, but fell in response to ileal distension. A well-known clinical observation, however, is that in a barium enema the contrast medium may reach into the distal ileum, i.e. the ileocaecal sphincter is not reflux-proof.

The most common defect of continent caecal reservoir for urine has been leakage due to malfunctioning nipple valve. In such cases the reservoir usually is continent at low filling, but at larger volumes with high intermittent tension of the bowel wall, sliding of the nipple valve may occur and leakage ensue. At revision of the nipple valves in such patients, sliding of the valve on the mesenteric border was found.

The recorded dynamics of the urinary caecal reservoir differed between patients who occasionally experienced leakage at high-volume filling and those with well-functioning valves. In the former patients the pressure waves in the outlet peaked later than the simultaneously initiated pressure waves in the reservoir. This implies risk of negative closure pressure, i.e. that the intrareservoir pressure for some space of time is higher than the outlet pressure. In addition, the duration of the pressure waves in the nipple valves was longer in these patients. A possible explanation of such findings is instability of the nipple valve, with sliding of the bowel layers during contractions. The peak of the pressure wave may not be reached until the sliding process stops. The presence of the ileocaecal sphincter in our patients apparently did not influence the propagation of bowel-wall tension in proximal direction.

The pressure waves that occurred intermittently in the full or near-full urinary caecal reservoir did not differ in amplitude from those recorded in ileal reservoirs for urine (Norlén & Trasti, 1978) or for intestinal contents (Akwari *et al.*, 1980). With lengthening time from construction of the caecal reservoir, our patients showed adaptation towards larger functional capacity. In regard to motor function, the caecal reservoir seems to be equivalent to the ileal reservoir for continent urinary diversion, and the caecal reservoir is certainly easier to construct.

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III

Acute Effects of Full Urinary Bladder and Full Caecal Urinary Reservoir on Regional Renal Function

A study with scintillation camera renography

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Abstract

Scintillation camera renograms were recorded in six patients without a history of bladder function disturbances and in eight patients with caecal urinary reservoir. Each patient was studied once with empty bladder/reservoir and once with full bladder/reservoir. Renograms were obtained from parenchyma, pelvis and whole kidney. Time was measured from injection of isotope to peak of the renogram curve ($T_{\max}$) and to the point corresponding to the centre of gravity of the area under the curve (T_g). A full reservoir gave longer $T_{\max}$ and T_g for both parenchyma and pelvis than an empty reservoir. With full bladder the only significant change was T_g increase for renal pelvis. In the patients with full caecal reservoir, the elimination of radioisotope from the renal pelvis was significantly slower, reflected as longer $T_{\max}$ and T_g , than in the subjects with full bladder. In comparisons between empty and full bladder/reservoir, T_g permitted clearer separation between the groups than did $T_{\max}$. The higher $T_{\max}$ and T_g values for full than for empty reservoir indicated obstruction to urinary flow and could be ascribed to the high intrareservoir pressure. Regularly occurring pressure waves with amplitudes of 30–65 cm H₂O were recorded in the reservoirs, sometimes reflected as transient increases in radioisotope activity in the renograms. In some patients the two kidneys differed considerably in their response to a full urinary bladder or reservoir. The cause may have been difference in the dynamics of the two ureterovesical junctions or of the uretero-intestinal anastomoses. It is concluded that the full urinary bladder exerts little influence on renal parenchymal and pelvic functions, as measured by scintillation camera renography, but that a full caecal urinary reservoir considerably slows the passage of the radioisotope.

An all-important requirement for success in permanent urinary diversion is the preservation of renal function. Impairment of renal function may arise from obstruction of the urinary flow, usually as a result of stricture of the uretero-intestinal anastomosis (15, 26). Low-pressure reflux of infected urine may also damage renal function (2, 23). Even if stricture and reflux can be avoided, high pressure in a urinary conduit or reservoir can adversely affect

renal function by impeding drainage of the upper urinary tract. Pressures in full ileal and caecal reservoirs may be high (10, 20). Fullness of the urinary bladder can lead to dilatation of the upper urinary tract (8,19), but its immediate influence on renal function is incompletely known.

The present experiments were made to observe if acute increase of the volume and pressure in caecal reservoirs for urine could produce a renographic pattern of obstruction, and if in this respect the caecal reservoir differs from the urinary bladder.

Materials and Methods

Two groups of patients were studied. The first group consisted of eight men with mean age 55 years (range 38–65). As part of the treatment for invasive bladder carcinoma, urinary diversion via a continent caecal reservoir had been accomplished 3–53 (mean 26) months previously. The construction of this involved isolation of the distal 20 cm of the ileum, the caecum and part of the ascending colon. Bowel continuity was restored by end-to-end ileocolic anastomosis. The appendix was removed. The ureters were implanted using a combination of two anti-reflux techniques, viz. a 3–4 cm long submucous tunnel (9) and a split-cuff ureteric nipple (28). The continence-providing mechanism was a 5 cm long intussuscepted ileal nipple valve, positioned in the distal part of the ileum, just proximal to the ileocaecal sphincter. The ileum was brought out through the rectus muscle. The nipple base was anchored to the abdominal wall and a stoma flush with the skin was fashioned (17). By insertion of a catheter at three to five-hourly intervals, the patient empties the reservoir. In between, the stoma is covered by a gauze pad only.

Six of these patients had received post-diversion, pre-cystectomy adjuvant radiotherapy. One man had reflux from the reservoir to the left renal pelvis following reimplantation of the ureter as a result of stricture. The other patients in the reservoir group had no roentgenologic signs of reflux.

The second group was the reference group. It comprised five men and one woman with mean age 53 years (range 42–65) without a history of bladder function disturbances. They had undergone transurethral resection of small superficial bladder tumours more than three months before the present study, at the time of which they were symptom-free. Five of them were studied with cystometry and micturating cystography. Cystometry showed slight instability at large filling of the bladder in one patient and cystography revealed distal reflux to a non-dilated ureter at micturition in another. In the other patients, the investigations were normal.

Intravenous urography before the study showed non-dilated upper urinary tracts in all patients. One patient in the reservoir group, however, had a urographically nonfunctioning kidney. Each patient was studied twice, with an interval of a few days, with scintillation camera renography. Each renography was performed with the bladder/reservoir either empty or full, in a randomized order. The study was approved by the Ethical Committee of the University of Lund.

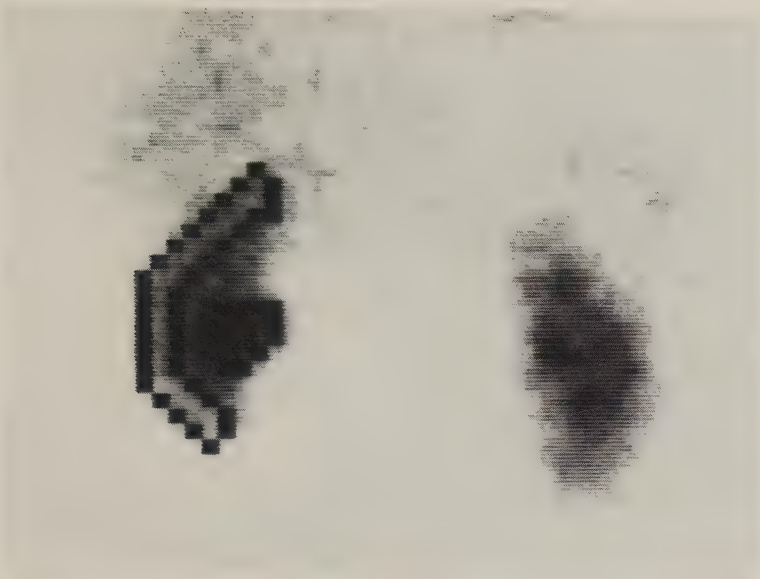


Fig. 1. Selection of parenchymal and pelvic regions for generation of renogram curves in the right kidney.

Scintillation camera renography

The technique was essentially as previously described (3). The scintillation camera had a 40 cm field of view (Maxicamera, General Electric) and was connected to a digital computer with magnetic disc data storage (PDP 11/34 computer with Gamma-11 analysis system, Digital Equipment Corp.).

The camera was equipped with a low energy, high resolution collimator. The patients drank one litre of water 60 to 30 minutes before injection of the radioisotope. They were investigated in upright sitting position, with the scintillation camera viewing the back. $^{99}\text{Tc}^{\text{m}}$ -DTPA (Diagnostic Isotopes Inc., 75 MBq, 2 mCi) was given by rapid intravenous injection.

Dynamic measurements were performed during 18 minutes, with 56 frames (30 of 10 sec duration followed by 26 of 30 sec duration) collected in a matrix of 64 x 64 picture elements. Renal parenchyma, renal pelvis and whole kidney were studied. A representative region for renal parenchyma was selected manually from a reconstructed 60-second image at approximately 2 to 3 minutes after the injection. It was chosen as a narrow band to avoid the calyces. From the same image was also selected an area comprising the whole kidney. The region for pelvis was selected from a 240-second image at approximately 14 to 18 minutes, chosen to represent pelvis only, though some overlying parenchyma may sometimes have been included (Fig. 1). A background count area was defined between the kidneys. Time-activity curves (regional and whole kidney renograms) were generated.

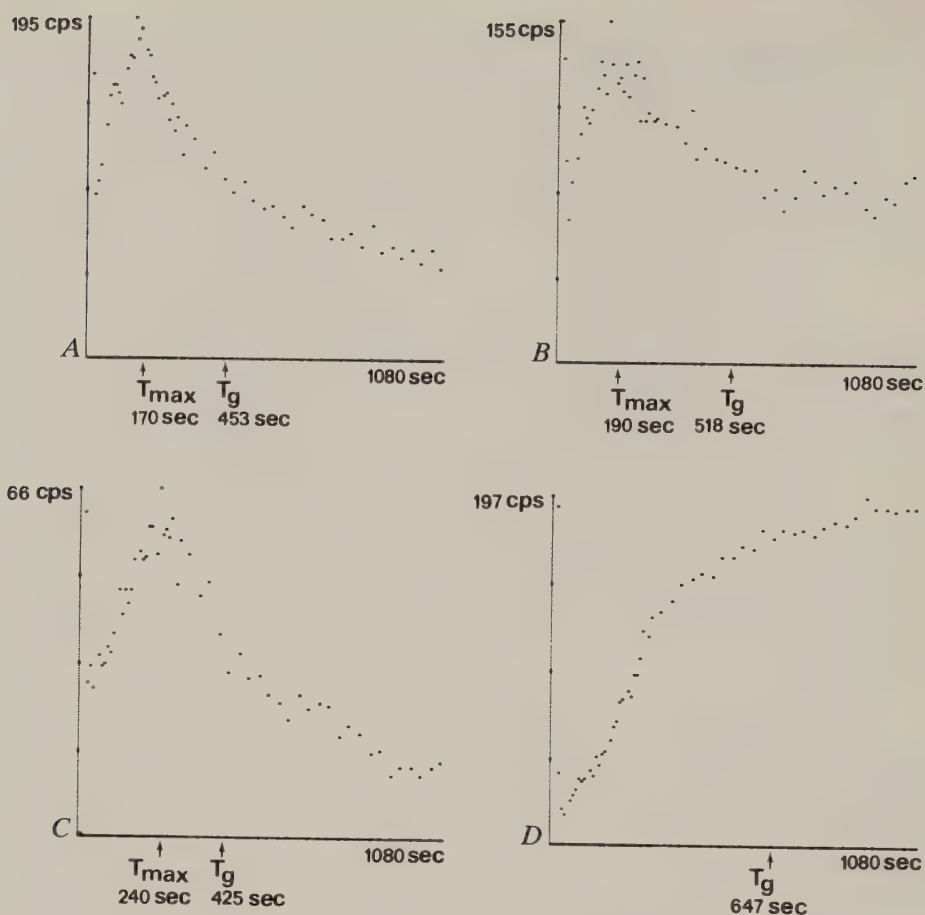


Fig. 2. Renogram curves from the right renal parenchyma in a 51-year-old man with empty reservoir (A) and with full reservoir (B). The curve from the renal pelvis with empty reservoir (C) shows normal passage of the radioisotope, while this passage is considerably delayed with full reservoir (D).

To characterize the time course of isotope passage through the different regions, two time intervals were determined in each curve after background subtraction. One interval was the time from injection of isotope to peak of the curve ($T_{\max}$). The other was the interval from injection of isotope to the time corresponding to the centre of gravity of the area under the curve during 18 minutes (T_g). These definitions are illustrated in Fig. 2. T_g was used instead of mean transit time because calculation of the latter can be valid only if there is a well defined terminal exponential fall in isotope activity, permitting extrapolation to zero activity, whereas calculation of T_g is totally independent of curve shape.

In the reference group 12 kidneys were analyzed. In the reservoir group 15 whole kidney curves were analyzed, but the regional renograms were satisfactory for analysis in only 11 kidneys, due to movement artifacts in the investigation of one patient and computer error in another.

Studies with empty bladder/reservoir were performed with a draining catheter in situ.

In six patients with a reservoir and in three with intact bladder, studies with full bladder/reservoir were done with *isobaric volume registration* (7). Via a catheter (16 F, All Silicone Foley, Dover), the bladder/reservoir was connected to a vessel with a large cross-sectional area (660 cm²) containing sterile water of 37°C. A baby-feeding catheter (8 F) was inserted alongside the 16 F catheter and connected via a pressure transducer (746, Siemens) to a recorder (Mingograph 803, Siemens-Elema) for continuous recording of the pressure in the bladder/ reservoir. The vessel was placed on an electric balance connected to the recorder. The rectal pressure, regarded as representing the intra-abdominal pressure, was measured via a balloon catheter. By subtraction of the rectal pressure from the total bladder or reservoir pressure, the pressure generated by the detrusor or the reservoir wall was obtained. The level of the vessel's water surface was increased stepwise above the level of the bladder, taken as the symphysis pubis, or of the reservoir, taken as a point halfway between the symphysis pubis and the stoma.

For the bladder we sought a pressure just below the micturition threshold and for the reservoir a pressure just below that at which the patient experienced need for emptying. Because of the large surface area of the vessel, volume variations did not significantly change the imposed hydrostatic pressure. The volume variations in the bladder/reservoir were recorded as weight changes of the vessel.

In five patients isobaric volume registration could not be accomplished for technical reasons. In three of these patients the bladder was filled with a syringe through the 16 F catheter, which was then clamped. In two reservoir patients, the reservoir was filled by diuresis before the examination.

Statistical methods

Student's t-tests for paired and unpaired observations were used for the statistical analyses. Differences with $p < 0.05$ were considered to be statistically significant.

Results

Values for $T_{\max}$ and T_g are shown in Table I and Fig 3. Lower values indicate more rapid passage or more efficient washout of the indicator. The following comparisons were made.

Full v. empty reservoir

$T_{\max}$ in the renal pelvic curves was considerably greater with full than with empty reservoir ($p < 0.01$). Three pelvic curves in two patients with full reservoir rose continuously during the 18-minute (1080 sec) measurement (Fig. 2). In these cases a $T_{\max}$ value of 1080 sec was used for the calculations.

$T_{\max}$ in the parenchymal curves was moderately longer with full than with empty reservoir (not statistically significant).

T_g for pelvic and parenchymal curves was significantly longer with full than with empty reservoir ($p < 0.001$ and $p < 0.05$, respectively).

Full v. empty bladder

No significant differences were found in $T_{\max}$ for either the pelvic or the parenchymal curves from full compared with empty bladder. T_g in the pelvic curves was slightly prolonged ($p < 0.05$) when the bladder was full. T_g in parenchymal curves was practically identical with full and with empty bladder.

Full reservoir v. full bladder

$T_{\max}$ in the pelvic curves was significantly longer in measurements from full reservoir than in those from full bladder ($p < 0.01$). In the parenchymal curves there was no significant intergroup difference in $T_{\max}$. T_g in pelvic and in parenchymal curves was significantly longer with full reservoir than with full bladder ($p < 0.001$ and $p < 0.05$, respectively).

Empty reservoir v. empty bladder

No significant differences in $T_{\max}$ or T_g were found for pelvic or for parenchymal curves when empty reservoir was compared with empty bladder.

Whole kidney v. parenchyma and pelvis

$T_{\max}$ and T_g values for whole kidney were intermediate in relation to those for parenchyma and pelvis. With full bladder and reservoir, however, the renographic curves for whole kidney became more similar to those for pelvis. The p-values for the differences between empty and full bladder/ reservoir were similar for whole kidney and pelvis.

Table I. Time intervals (sec) obtained from regional and whole kidney renograms (mean+SEM)

		Renal parenchyma		Renal pelvis		Whole kidney	
		T_{max}	T_g	T_{max}	T_g	T_{max}	T_g
Bladder (n=12 tests)	empty	160±8	448±9	203±12	466±9	188±11	458±9
	full	192±11	451±9	288±36	498±14	223±14	480±11
Reservoir (n=11 for parenchyma & pelvis, n=15 for whole kidney)	empty	165±7	440±22	260±30	499±19	211±10	468±14
	full	282±69	504±22	615±95	619±23	546±91	566±17

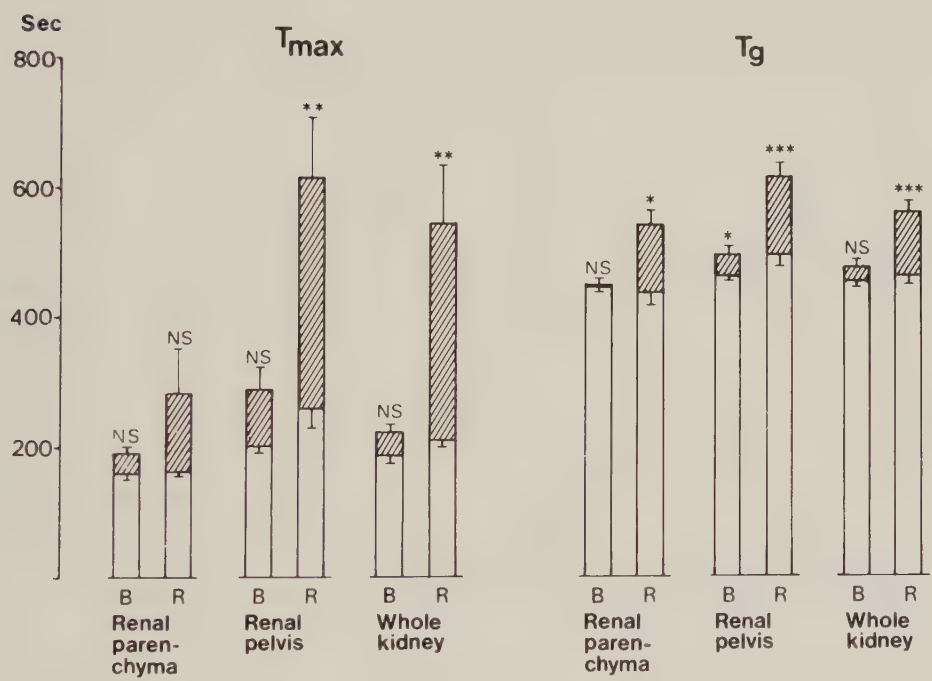


Fig. 3. Mean values for time to peak (T_{max}) and time to centre of gravity of the area under the curve (T_g) in regional and whole kidney renograms. Total height of bars indicates values with full bladder (B) or reservoir (R). Open bars indicate empty bladder or reservoir. SEM is indicated. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Differences between the two kidneys

The passage of radioisotope through the two kidneys was not always identical. Such differences were seen both in the presence of a normal bladder (Fig. 4) and when there was a caecal urinary reservoir (Fig. 5) Fig. 5 A shows a normal renogram curve for the parenchyma of the left kidney in a patient with full reservoir. This ureter had been reimplanted with end-to-side anastomosis two years previously, due to stricture, and exhibited free reflux. On the right side, the uretero-intestinal anastomosis had been performed with anti-reflux technique (3–4 cm long submucous tunnelling of the ureter + split-cuff ureteric nipple). Fig. 5 B shows an almost continuously rising curve for the parenchyma of the right kidney.

Pressure in full bladder and full reservoir

The recorded detrusor pressures were within the normal range (Table II). While the basal pressure in the full reservoir was low, the intermittent pressure waves were of high amplitude (Table III). The pressure waves were in two patients sometimes reflected as transient increases in the radioisotope activity of the descending limb of the pelvic renogram curve (Fig. 6). No correlation was found, however, between pressure wave amplitude and $T_{\max}$ or T_g .

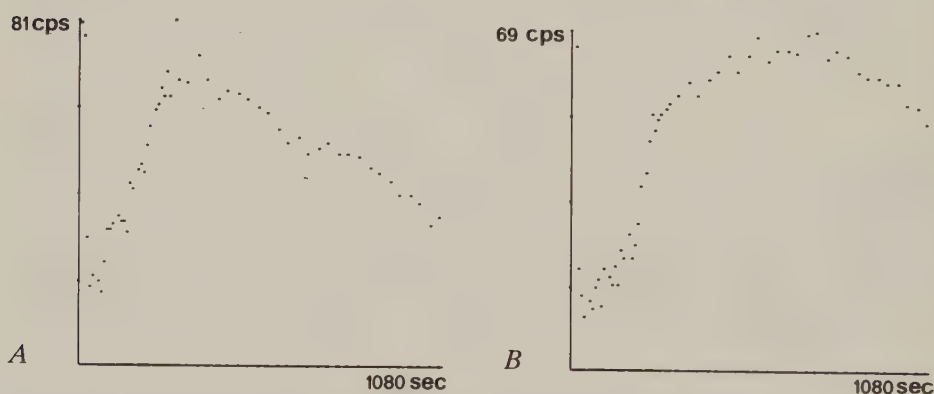


Fig. 4. Renogram curves from the left renal pelvis (A) and the right renal pelvis (B) in a 43-year-old man with full urinary bladder.

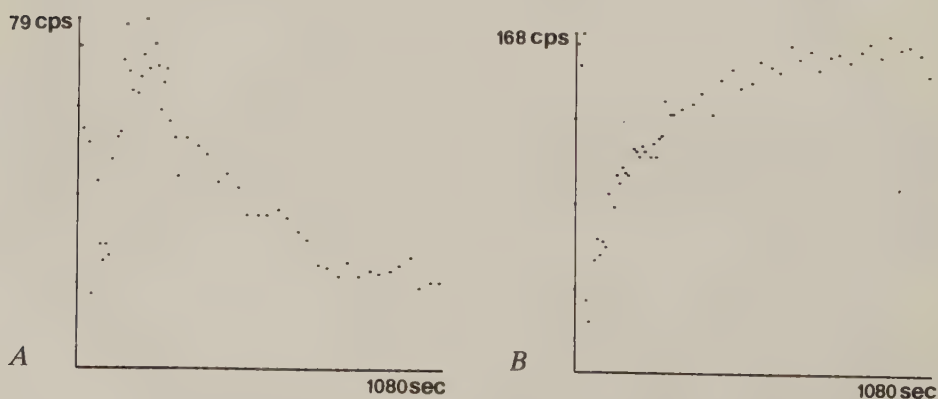


Fig. 5. Renogram curves from the left renal parenchyma (A) and the right renal parenchyma (B) in a 58-year-old man with a full caecal urinary reservoir.

Table II. Urinary bladder volume and detrusor pressure during scintillation camera renography (18 min) in patients with full bladder.

Patients (sex, age)	Volume (ml)	P_{det} (cm H ₂ O)
M 65	285	10
M 62	195	5
F 43	360	7
M 47	590	7
M 42	520	16
M 59	400	6

Table III. Reservoir volume, basal pressure and pressure waves (number, amplitude and duration) in full caecal urinary reservoir during scintillation camera renography (18 min).

Patients (sex, age)	Volume ml	Basal pressure cm H ₂ O	No of pressure waves	Amplitude of pressure waves cm H ₂ O (mean±SEM)	Total duration of pressure waves, % of 18 min
M 62	300	4	9	50±1	37
M 51	610	9	8	30±4	33
M 38	650	15	8	65±5	41
M 61	415	13	6	38±1	29
M 65	*	4	5	34±3	15
M 58	550	10	6	30±2	18
M 54	235	11	9	32±4	28
M 51	410	17	7	39±3	23

* leakage

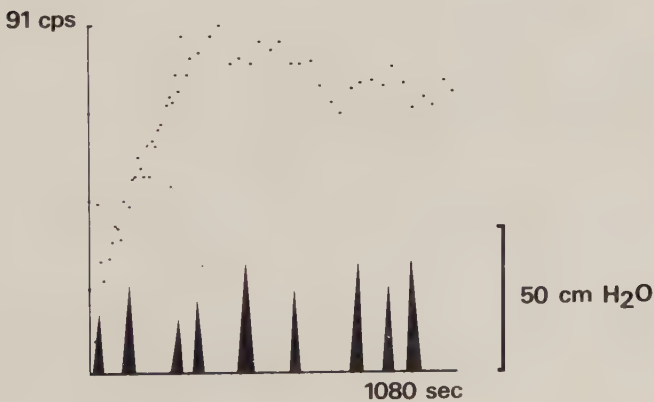


Fig. 6. Renogram curve from the right renal pelvis in a 54year-old man with full caecal urinary reservoir. Amplitudes of intermittently occurring pressure waves in the reservoir are indicated.

Discussion

The influence of bladder filling on the upper urinary tract has been recognized since the introduction of intravenous urography. Thus Roseno stated in 1929 (24) that infusion of contrast medium should be done when the bladder is full, to improve filling and visualization of the renal pelvis and the ureter. The danger of misinterpreting a dilated renal pelvis and ureter as pathologic, by overlooking the possibility of a full bladder as the cause of the dilatation, has been pointed out (8, 19).

Ureteral pressure has been shown to increase with filling of the bladder (5,31). High diuresis with full bladder was reported to raise the intrapelvic pressure more than bladder distension only (12). These studies, however, did not include renal function.

To investigate the effect of bladder/reservoir filling on the upper urinary tract, we used scintillation camera renography. This technique has become an important tool for evaluating renal function. It has been used to determine individual kidney function (3, 6, 14, 21, 22). Another important application is in the evaluation of urinary obstruction (1, 4, 13 25). Scintillation camera renography permits detailed functional analysis by the generation of regional renograms from parenchyma, pelvis, etc. It is then possible to determine if there is an obstructive uropathy only, or if in addition nephron function is jeopardized, i.e. there is obstructive nephropathy (11, 29, 30).

The renograms with empty bladder and empty reservoir were of normal appearance (Fig. 2), indicating that none of the examined patients had obstruction either in the ureter or at the uretero-vesical junction/ uretero-intestinal anastomosis. Urography, moreover, had shown nondilated upper urinary tracts. When the examination was repeated with full bladder, the passage of the radioisotope through the renal pelvis was slightly slower. This accords with the mentioned observations of dilatation of the upper urinary tract and raised ureteral pressure when the bladder is full. Parenchymal passage of radioisotope was not affected, on the other hand.

The most striking finding in the present experiments was the greatly delayed passage of the radioisotope through the renal pelvis in patients with full caecal reservoir. Indeed, in two of these patients three pelvic curves continued to rise throughout the measurement. The large increases found in $T_{\max}$ and T_g indicated obstruction which may be regarded as functional as it was absent or less obvious both at renography with empty reservoir and at urography. Although in renal parenchyma the increase of $T_{\max}$ and T_g was of smaller degree, parenchymal transit of the radioisotope was slower with full reservoir than with full bladder.

The functional obstruction probably was related to the pressure characteristics of the full caecal urinary reservoir. As the basal pressure of the full reservoir was comparable with the detrusor pressure of the full bladder, the basal pressure itself could not explain the renographic pattern given by the full reservoir. However, intermittent contractions of the reservoirs were seen, with large pressure amplitudes, and these could conceivably have contributed to the functional obstruction. In addition, identical pressures may have had different

effects on the uretero-vesical junctions than on the uretero-caecal anastomoses, causing greater resistance to urine flow into the caecal reservoir than into the bladder.

In some patients the renograms of the two kidneys differed appreciably in their response to a full bladder or reservoir. Such differences support the view that factors other than the pressure per se may be important, e.g. the shape of the uretero-vesical junction/ureteral implantation. It has been suggested that bladder distension gives rise to stretching of the trigonal musculature or ureter, which in turn can obstruct the transportation of urine through the intramural part of the ureter (27). The tension of the bladder wall can increase considerably when the bladder is filled, even though the detrusor pressure remains low (18).

In the patients with full intact bladder, differences between the two kidneys (Fig. 4) may have been due to differing length of the intravesical ureter or to changes in the adjacent bladder wall, e.g. secondary to previous transurethral resection. In patients with reservoir, similar factors could have been valid concerning the uretero-intestinal anastomosis. Thus, resistance to flow may be higher in a ureter that traverses the reservoir wall obliquely (e.g. through a submucous tunnel) than in a ureter that passes perpendicularly through the wall (Fig. 5). Transient increases in radioisotope activity in the renogram curves for pelvis appeared concomitantly with or shortly after the reservoir contractions in two patients (Fig. 6). These increases probably were due to intermittent episodes of functional obstruction caused by the reservoir contractions, as no urographic evidence of reflux had been found in the patients.

Conceivably, the reservoir contractions with high intrareservoir pressure could adversely affect renal function in the long run. However, glomerular filtration rate (GFR) in these patients was well preserved and compared favourable with GFR in patients with conduit urinary diversion after a mean follow-up of three years (16).

Two different parameters, $T_{\max}$ and T_g , were used in this study to describe the transit of the radioactive indicator through the kidney. Of the two, $T_{\max}$ is easier to determine in a renogram, and it is conventionally used in clinical renography. In this study the direction of change was always the same for $T_{\max}$ as for T_g (Table I, Fig. 3). Usually $T_{\max}$ changed more than T_g . On the other hand, when significant differences were found in the various comparisons, the p-values were lower for T_g than for $T_{\max}$. Thus in the present experiments T_g permitted clearer separation between the groups than did $T_{\max}$. The probable reason was that the computation of T_g utilized the entire renographic curve, whereas $T_{\max}$ represented a single point on the curve.

In conclusion, the present study showed that a full urinary bladder exerted little influence on renal parenchymal and pelvic function as measured by scintillation camera renography. On the other hand, fullness of the caecal urinary reservoir considerably delayed the passage of the radioisotope.

Acknowledgement

This investigation was supported by the Swedish Medical Research Council Grant No B81-29X-2872-12C.

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IV

Renal Function after Urinary Diversion

A study of continent caecal reservoir, ileal conduit and colonic conduit

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Abstract

Total and separate renal function, renal parenchymal thickness and dilatation of the upper urinary tract were studied in 40 patients preoperatively and 24 to 67 months after urinary diversion, using Cr-EDTA clearance test, scintillation camera renography and urography. In ten patients a continent caecal reservoir was used for diversion. In the other patients, an ileal or a colonic conduit (15 patients with each method) was used, one ureter being implanted with an anti-reflux method and the other with direct technique. Renal function following urinary diversion showed little or no deterioration in most patients. The functional outcome was not related to the method of diversion or, in the conduit groups, to the mode of ureteral implantation. Serum creatinine tests and urography were not adequate for determining loss of renal function. Radionuclide studies proved to be valuable for assessing renal function after urinary diversion.

The concept of external urinary diversion via a continent reservoir has intrigued surgeons since the early years of this century (27, 44). Interest has increased in the past decade. Favourable functional results have been reported from use of ileum and caecum as reservoirs (4, 5, 25). Technical complexity, however, has limited the use of such reservoirs in clinical practice.

The most widely used method for urinary diversion is still the ileal conduit. But it has become obvious that this method is associated with high morbidity and that the long-term results in regard to renal function are less satisfactory than was once thought (28, 31, 32, 33, 35, 37, 40). Reflux has been considered an important cause of renal deterioration with passage of time (6, 31, 39), and non-refluxing uretero-intestinal anastomoses into ileal or colonic conduits were claimed to give superior results (1, 2, 41). Comparisons between reports are difficult, however, as the respective series often differ concerning age, underlying disease, concomitant surgery, radiotherapy, length of follow-up, etc. We started a prospective study 1977 to evaluate if the choice of conduit (ileum or colon) and the technique of uretero-intestinal anastomosis (direct or anti-reflux) in time influenced renal function.

The present report concerns renal function after urinary diversion via a continent caecal reservoir, and also presents preliminary results from the mentioned prospective study of conduit diversion.

Material and Methods

Patients

In the period 1977–1980, 55 patients underwent procedures for urinary diversion (Table I), and 40 of them have been followed up for at least two years. The indication for diversion was high-grade, invasive bladder carcinoma in 51 patients. Most of these patients received combined treatment, with adjuvant radiotherapy after the diversion and before cystectomy. Irradiation was begun three to four weeks after the diversion, with 45 Gy over four weeks or 20 Gy over five days. Cystourethrectomy was performed four weeks after termination of the 45 Gy course or a few days after 20 Gy. Neurogenic bladder disorder was the reason for urinary diversion in four patients.

A continent caecal reservoir was constructed in 12 of the 55 patients. Both ureters were implanted with anti-reflux technique. An intussuscepted nipple valve was created in the ileal outlet to achieve continence (29). In the other 43 patients an ileal or a colonic conduit was used for urinary diversion. One ureter was implanted with anti-reflux, and the other with direct technique. The intention was to randomize preoperatively the type of conduit and which ureter would be implanted with anti-reflux technique. During the operation, however, the random allocation could not be strictly adhered to. Thus, in six patients allocated to colonic conduit, ileal conduit had to be performed instead, due to findings such as colonic diverticula. To obtain a reasonably balanced distribution between the groups actually receiving the two types of conduit, each patient following a case in which an unplanned ileal conduit had been performed was allocated to the colonic group. Of the 43 patients, 23 received an ileal conduit and 20 a colonic conduit (sigmoid colon was used in 15 and transverse colon in 5 patients).

Operative technique

The following methods of uretero-intestinal anastomosis were employed. Caecal reservoir, anti-reflux anastomosis: Submucous tunnel (20) combined with a ureteric split-cuff nipple (43).

Ileal-conduit, anti-reflux anastomosis: Ureteric split-cuff nipple.

Ileal conduit, direct anastomosis: Open technique (42).

Colonic conduit, anti-reflux anastomosis: Submucous tunnel (20, 26).

Colonic conduit, direct anastomosis: Open technique.

Polyethylene tubes, Fr 5 or 8 (Beyersdorf, Mölndal, Sweden) were used as stents in all cases. They were removed after about ten days.

Evaluation

In the present study, postoperative complications were classified as those occurring before cystectomy in the patients who received combined treatment, and those occurring during the hospital stay in the other patients. As late complications were considered those thereafter occurring, until death or the end of follow-up. The evaluation of renal function included only the 40 patients followed up for at least two years. For urinary diversion a continent caecal reservoir had been constructed in 10 of these patients, an ileal conduit in 15 and a colonic conduit in 15. The mean observation time for the three subgroups was 43, 36 and 36 months, respectively.

Table I. Survey of 55 patients subjected to urinary diversion by means of continent caecal reservoir, ileal conduit or colonic conduit.

Diversion procedure	No of patients	Sex		Age (yrs)		Diagnosis		Post-diversion			Follow-up ≥2 yrs
		F	M	range	mean	bladder cancer	neurogenic bladder disorder	radiotherapy 20 Gy	45 Gy	Cyst- ectomy	
Caecal reservoir	12	1	11	38–62	54	12	–	6	4	11	10
Ileal conduit	23	4	19	34–70	56	21	2	13	6	19	15
Colonic conduit	20	8	12	42–68	60	18	2	8	4	17	15

Renal function

Renal function studies included total and separate glomerular filtration rate (GFR) and serum creatinine. Total GFR (ml/min) was obtained as the total plasma clearance of ⁵¹Cr-EDTA with a single-injection method (8). The relative renal function in each patient (%) was expressed as the ratio of the measured GFR (ml/min per 1.73 m²) to the corresponding age-dependent normal GFR (21), the ratio being multiplied by 100. Moderate impairment of renal function was defined as 75–52% (10). Separate GFR was obtained by scintillation camera renography, essentially as previously described (7). The radiopharmaceutical used in most of the investigations was ⁹⁹Tc^m-DTPA, but in ten preoperative studies ¹³¹I-Hippuran was used. The two agents give the same result for separate renal function (7). Serum creatinine was determined with a modified picric acid method (22). The radionuclide studies were performed preoperatively, 3 to 6 months postoperatively, and thereafter yearly. For the final evaluation we used the latest measurements. They were obtained 24 to 67 months after urinary diversion.

Urographic appearance of kidneys and upper urinary tract

A preoperative intravenous urography was used as reference. The film then obtained after release of the ureteral compression was compared with films taken after the diversion procedure. The width of the ureter and the renal pelvis was classified in one of the four stages, normal, slightly dilated, moderately dilated or severely dilated. A significant change was considered to have occurred in kidneys that had bypassed one stage. In addition, we considered complete cessation of function as a significant change. Presence of calculi and signs of pyelonephritis were recorded. To evaluate changes in renal parenchymal thickness, the distance from the papilla of a major calyx in the upper, middle and lower zone to the surface of the kidney on an anteroposterior view was measured and was compared with the same distance at postoperative examinations.

Evaluation of reflux to the upper urinary tract

Presence of reflux was investigated with "loopography". With the patient mildly dehydrated and in supine position, a Foley catheter 16F was inserted into the conduit. Contrast medium (Isopaque Cysto®, Nyegaard, Oslo, Norway) was allowed to drip in by gravity from a height of 75 cm and at a speed of approximately 5 ml/min. The examination was monitored by intermittent

fluoroscopy. If reflux was not seen after 10 minutes, the conduit was occluded by inflating the balloon of the catheter and the infusion was continued until reflux occurred or the patient experienced discomfort.

Loopography was performed in 11 patients with ileal conduit and in 14 with colonic conduit, all of whom had been observed for at least two years postoperatively. "Reservoirigraphy" was performed in all the ten patients with caecal reservoir who had at least two years follow-up, as described elsewhere (29).

Statistical methods

The t-test, two-sample t-test and one-way analysis of variance were used for making the statistical inferences.

Results

Morbidity and postoperative mortality

The postoperative complications and the late complications are listed in Table II. A detailed description of these complications is beyond the scope of this presentation. In the conduit patients the complications did not differ from those in other, similar series. No correlation was found between complications and type of conduit or of uretero-intestinal anastomosis. A detailed account of the caecal reservoir has been presented for publication (29).

Two patients died postoperatively. In both of them, cystectomy without preceding irradiation had been performed simultaneously with colonic conduit diversion. One of the patients never regained consciousness after surgery, and showed neurologic signs compatible with apallic syndrome. The other patient died after two months. A pelvic abscess was drained postoperatively, but his condition deteriorated. Autopsy revealed extensive metastatic urothelial malignancy.

Renal function

Among the 40 patients followed up for at least two years, 12 were found at the latest examination to have moderately impaired renal function relative to age and body size. In eight of these patients the serum creatinine concentration was within normal range (60–115 $\mu\text{mol/l}$). In addition, one patient had a severely decreased renal function, 20% of normal GFR.

Total GFR was unchanged at follow-up compared to preoperative value, in the patients with continent caecal reservoir (Table III). In the patients with ileal conduit or colonic conduit there was moderate decrease of GFR ($p < 0.01$ and $p = 0.05$, respectively). In analysis of variance, however, there was no significant difference in the GFR change between the three groups.

Separate GFR showed non-significant reduction in both conduit groups when the preoperative and postoperative values were compared. Neither the technique of ureteral implantation nor demonstrable reflux at loopography significantly influenced the magnitude of the change in separate GFR.

At follow-up examination (Table IV), total GFR had fallen by at least 20 per cent in eight patients. Separate GFR was reduced in 23 kidneys. A 40 per cent or greater loss of renal function occurred in 2 of the 20 kidneys in the caecal reservoir group, in 6 of the 30 kidneys in the ileal, and in 3 of the 30 in the colonic conduit group.

Table II. Postoperative and late complications after urinary diversion (number of patients).

	Method of diversion		
	Continent caecal reservoir	Ileal conduit	Colonic conduit
<i>Postoperative complications</i>			
Deaths			2
Insufficiency of intestino-intestinal anastomosis	1		
Necrosis of conduit			1
Impaired circulation to reservoir outlet	1		
Torsion of conduit+obstruction of uretero-intestinal anastomosis		1	
Insufficiency of uretero-intestinal anastomosis			1
Urinoma	1		
<i>Late complications</i>			
Stricture of uretero-intestinal anastomosis	3	2	2
Renal stone requiring surgery		1	1
Renal stone not requiring surgery		2	
Reservoir stone	3		
Stoma retraction requiring surgery			1

Urography demonstrated significant changes, such as nonfunctioning kidney, parenchymal reduction with dilatation or renal scarring, or dilatation only, in 8 of the 11 kidneys with at least 40 per cent reduction of function. The other three kidneys had normal urographic appearance.

In four other kidneys, in which function was well preserved, urography showed significant changes. Thus in all of them there was 3 to 4 mm parenchymal reduction. Significant dilatation of the pelvis and ureter had occurred in three of the four cases; these ureters had been anastomosed with open technique.

When dilatation of the urinary tract developed, it did so within six months of the urinary diversion.

The loopographies in 11 patients with ileal conduit showed reflux only on the side with direct anastomosis in five patients, bilateral reflux in two patients and no reflux in four patients. In 14 patients with colonic conduit, the loopographies showed reflux only on the side with direct anastomosis in five patients and no reflux in nine patients. In the ten patients with caecal reservoir, no reflux was found at reservoirography after the primary operation, but reflux appeared in two patients after surgical revision, when direct anastomosis was performed on one side because of stricture.

Table III. Total and separate GFR, measured by $^{51}\text{Cr-EDTA}$ clearance and scintillation camera renography, preoperatively and ≥ 2 years after urinary diversion

Method of diversion	No of patients	No of kidneys	Follow-up (months)		$^{51}\text{Cr-EDTA}$ clearance (ml/min, mean $\pm$ SEM) at follow-up		
			mean	range	total preoperative	total	separate
Caecal reservoir, anti-reflux anastomosis	10	20	43	24-62	97 $\pm$ 6	97 $\pm$ 7	
Ileal conduit	15	30	36	24-59	100 $\pm$ 4	86 $\pm$ 7	
direct anastomosis							39 $\pm$ 5
anti-reflux anastomosis					47 $\pm$ 3		46 $\pm$ 6
					53 $\pm$ 3		
Colonic conduit	15	30	36	24-67	80 $\pm$ 5	72 $\pm$ 5	
direct anastomosis					43 $\pm$ 3		35 $\pm$ 4
anti-reflux anastomosis					37 $\pm$ 5		37 $\pm$ 3

Table IV. Decrease in total GFR and in separate kidney GFR in 40 patients 24-67 months after urinary diversion.

% decrease in $^{51}\text{Cr-EDTA}$ clearance	Caecal reservoir			Ileal conduit			Colonic conduit		
	patients <i>n</i> = 10	kidneys <i>n</i> = 20		patients <i>n</i> = 15	kidneys <i>n</i> = 15		patients <i>n</i> = 15	kidneys <i>n</i> = 15	
20-29	1	2		1	1	1	1	2	3
30-39				1	2	2	3		
40-49					3				1
≥ 50		2		1	1	2		2	

Discussion

In earlier studies the course of renal function after urinary diversion was evaluated from measurement of serum creatinine and urography. Both methods are imprecise for this purpose, however. Poor correlation was found between serum creatinine and renal function as measured by clearance technique (11). Serum creatinine within normal range does not preclude impairment of renal function. Thus, most of our patients with moderately decreased clearance values had normal serum creatinine. On the other hand, rise in individual serum creatinine levels during an observation period usually indicates impairment of renal function.

To achieve accurate assessment of total renal function, the GFR was measured as plasma clearance of $^{51}\text{Cr-EDTA}$, a test with high precision (9). Unilateral impairment of kidney function with contralateral compensatory increase can give unchanged total renal function. Separate renal function can be determined when scintillation camera renography also is employed (7, 14). This method can further yield useful information for evaluation of obstruction (12, 24), especially as regional functional analysis is possible (23, 45). Thus, with these diagnostic tools, the fate of individual kidneys can be studied.

Our investigation showed that renal function as a rule was well preserved 24 to 67 months after urinary diversion. The choice of method for diversion (continent caecal reservoir, ileal or colonic conduit) did not influence renal function. Nor did the type of uretero-intestinal anastomosis in the patients with conduit (direct or anti-reflux anastomosis).

Three main factors are generally considered to be responsible for damage to renal function after urinary diversion. They are obstruction, reflux and infection.

Obstruction due to stricture of the uretero-intestinal anastomosis appearing later than six months after diversion operation was not seen in this study, though it was previously described (28, 37). However, the performance of urinary diversion before radiotherapy may have lessened the risk of late complications. Strictures requiring surgical revision or giving non-functioning kidney at follow-up examination were in all cases preceded by urographic dilatation of the ureter and pelvis, and this dilatation occurred soon after the diversion. Stricture of the anastomosis thus probably was due to faulty surgical technique and/or impairment of blood supply. Strictures developed in all groups, and no single technique of uretero-intestinal anastomosis was free from this complication. As the anti-reflux techniques are more elaborate than the direct, reflux-permitting anastomosis, one might anticipate a higher incidence of strictures following anti-reflux procedures. No such higher incidence was found in the present cases. In another series, comprising 112 diversions by ileal conduit, into which the ureters were implanted with a ureteric split-cuff technique, stricture occurred in 10 per cent of the cases (18).

A long submucous tunnel in a colonic conduit has been reported to cause obstruction (3, 13). Other reports did not confirm this observation, however (1, 2). The technique used in the present reservoir group was a combination of ureteric split-cuff and submucous tunnel, i.e. a fairly complicated technique which might be expected to give a relatively high complication rate.

Obstruction may also be due to renal stone. This complication was seen in one patient in each of the conduit groups. Stones were formed in three of the caecal reservoirs. They caused no obstruction and were easily removed.

In patients with a continent caecal reservoir, functional obstruction to urine

flow occurs when the reservoir is full (30). At follow-up of these patients in the present study, however, little or no deterioration of renal function was found. Patients with a continent ileal reservoir for urine have likewise been reported to have well preserved renal function (25).

Reflux from ileal conduit with direct uretero-intestinal anastomoses can affect the long-term functional result (6, 39). Some surgeons have therefore abandoned this type of diversion for patients with long life-expectancy (31). Non-refluxing colonic conduits have been considered to give better kidney preservation (1, 2). There is experimental support for the importance of protection against reflux. Thus anti-reflux implantation of one ureter into a colonic conduit in dogs significantly lowered the incidence of pyelonephritis as compared with the other, freely refluxing side (15, 36). In children with an average follow-up of 13 years after colonic conduit diversion, urographic renal deterioration was found significantly more often when reflux was demonstrated in loopograms than when reflux was not seen (17). The present study showed no difference in preservation of renal function after follow-up for on average three years between kidneys protected against reflux and unprotected kidneys, irrespective of the type of conduit.

We found that loopography often failed to demonstrate reflux to ureters implanted with direct technique, especially in colonic conduits. Possible reasons were inadequate dehydration of the patient (16), peristaltic activity of the ureter, or incomplete filling of the conduit.

Theoretically, the proposed detrimental effect of reflux on renal function may be due to high pressure and/or infection. It is difficult to separate these causes clinically, however, especially since bacteriuria often is present in urinary conduits. A notable finding in the present study was that separate renal function did not change in the two patients with caecal reservoir who were followed up for 2 and 3 1/2 years after revision of the uretero-intestinal anastomosis on one side due to stricture using a direct technique (Fig. 1). Reservoirography after the reimplantation showed free reflux to the renal pelvis, but the patients have remained asymptomatic, despite the combination of relatively high pressure in the reservoir and presence of *Klebsiella* and *Escherichia coli* in the urine. In patients with intact bladder, reflux to the kidneys, if associated with infection, entails considerable risk of renal damage (19, 38).

Discrepancy between urographic observations and measurements of renal function was often observed in this study. Urograms could be normal even when there was considerable loss of glomerular function. Similar experience was reported by authors who estimated GFR in nine patients on average six years after urinary diversion with ileal conduit (34). They found low GFR in eight of these patients, but abnormal urography in only one. Urography thus can be regarded as a less satisfactory test of renal function.

When urography showed dilatation of the upper urinary tract, clearance study and renography often gave valuable information. Scintillation camera renography could show loss of separate renal function (Fig. 1). Regional functional analysis can reveal if dilatation represents an obstructive uropathy only, or an obstructive nephropathy, i.e. if nephron function is affected (23, 45). In the present study, urography showed dilatation of the upper urinary tract after urinary diversion in many patients, though several of them had preserved renal function. Dilated upper urinary tract thus was not synonymous with compromised renal function (Fig. 2). As long as the renogram curve for the parenchyma has a normal appearance, there is probably no indication for corrective surgery.

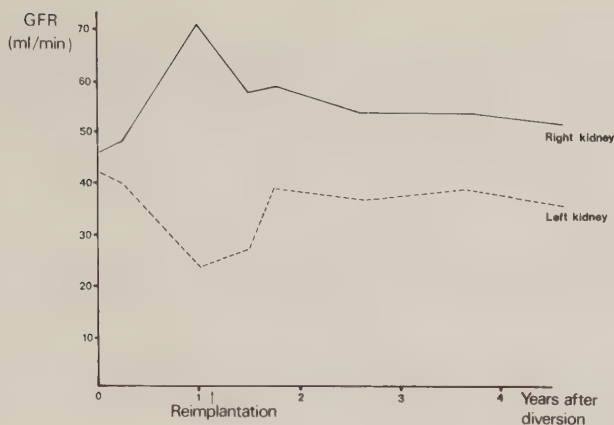


Fig. 1. Time course of separate glomerular filtration rate (GFR) in a 58-year-old man with urinary diversion via a continent caecal reservoir. Stricture of the left uretero-intestinal anastomosis necessitated reimplantation of the left ureter.

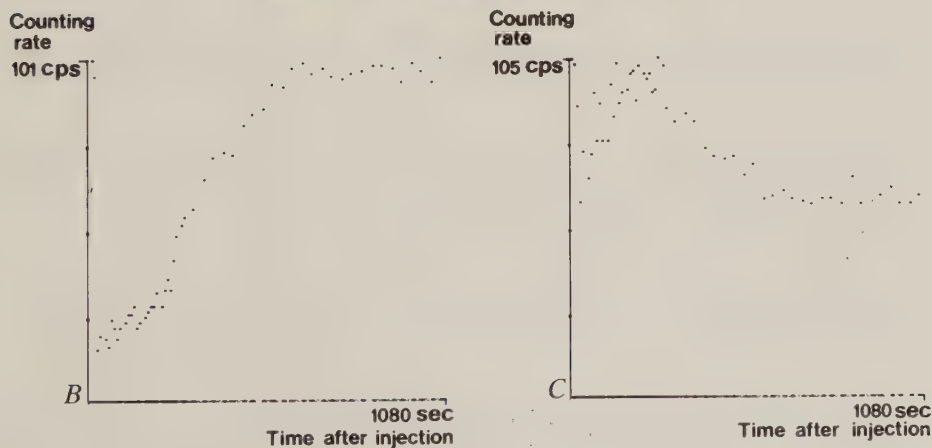
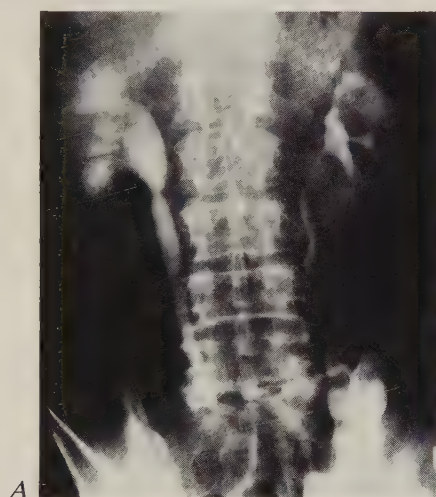


Fig. 2. Urography in a 65-year-old man one year after urinary diversion via colonic conduit (A). The right ureter was implanted with anti-reflux technique. The renogram curve for the right renal pelvis (B) rises almost continuously, while the curve for the right renal parenchyma (C) is of normal appearance.

Acknowledgement

This investigation was supported by grants from the Swedish Medical Research Council (B81-29X-2872-12C), and the Maud and Birger Gustavsson Fund, Stockholm.

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Immunoglobulins in Urine from Patients with Ileal and Colonic Conduits and Reservoirs

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Abstract

Gel chromatography of proteins in urine from continent cecal urinary reservoirs revealed abundance of high molecular weight proteins, especially secretory IgA (sIgA). Quantitation of immunoglobulins in urine from ileal and colonic conduits and ileal and cecal reservoirs showed sIgA, IgG and IgM in amounts considerably greater than in urine from normal urinary tracts. More sIgA was found in reservoir than in conduit urine, but there was no such difference for IgG and IgM. In hemagglutination-inhibition tests, IgA antibodies from cecal reservoir urine inhibited adherence of *Escherichia coli* to human and animal erythrocytes. High levels of sIgA may constitute a host defense mechanism against bacteriuria in urinary reservoirs and conduits.

Urinary diversion via an ileal conduit has been shown to entail considerable progressive risk of diminished renal function^{1,2}. Urinary tract infection is attributed importance in this process. In the absence of obstruction, however, clinical signs of infection are uncommon in these patients.

Although urinary reflux has been regarded as important in the same context^{3,4}, we found no difference in separate glomerular filtration rate between kidneys protected from reflux and unprotected kidneys after follow-up averaging three years⁵. Since reflux of infected urine is detrimental to renal function in patients with intact urinary tract^{6,7}, our observations suggest that protective mechanisms may be present in the urinary tract of patients with conduit urinary diversion.

Immunoglobulins, among which secretory IgA (sIgA) predominates, contribute to the host defense at the mucosal surfaces of the body. Factors as yet unknown are whether the production of immunoglobulins in an intestinal segment is altered when the segment is excluded to serve as a conduit or reservoir for urine, and how such exclusion affects the protective role of immunoglobulins in the segment.

In the present study we compared the concentrations of immunoglobulins in urine from continent cecal or ileal reservoir and from colonic or ileal conduit. The ability of sIgA to inhibit hemagglutination by *Escherichia coli* isolated from cecal reservoir urine or fecal samples was also tested.

Materials and Methods

Subjects

The study comprised 18 patients with urinary diversion and a man and a woman with normal urinary tract. Nine of the patients had a continent cecal reservoir⁸ and three a continent ileal reservoir⁹, while three had an ileal and three a sigmoid conduit (Table I). The respective ages of the normal controls were 46 and 41 years. The serum creatinine was within normal range (60–115 $\mu\text{mol/l}$) in all subjects.

Urine

Twenty-four hour samples were collected. In two patients with cecal reservoir, urine was collected on three additional occasions at one-week intervals. Sodium azide was added to the urine to a final concentration of 0.02M in order to prevent bacterial growth. The urine specimens were filtered at 4°C through filter paper (Whatman 1) to remove insoluble material. Urinary macromolecules were then concentrated 50 times in an Amicon ultrafiltration cell, model 12, with UM 20 membrane (retentivity MW > 20 000). Urine creatinine was determined by a modified picric acid method¹⁰.

Antisera

Rabbit antisera against sIgA, secretory component (SC), IgG and IgM (Dakopatts, Copenhagen, Denmark) were used.

Gel chromatography

Gel chromatography of urinary macromolecules was performed on Sephacryl S-300, 1.5 × 82 cm (Pharmacia Fine Chemicals, Uppsala, Sweden) in 0.1 M Tris-HCl buffer, pH 8.0. Concentrated urine (1 ml) was applied to the column and 3.6 ml fractions were collected. Total protein was measured by reading the absorbance at 280 nm. The distribution of sIgA and IgG and the possible presence of free SC in the effluent were determined with electroimmunoassay¹¹. IgM was assayed by single radial immunodiffusion¹². An agarose with low electro-endo-osmotic flow was used for determination of sIgA and free SC, with addition of 3% PEG 6 000 for SC determination. For approximate estimation of molecular size, polyacrylamide gel electrophoresis was used (PAA 4/30, Pharmacia Fine Chemicals).

Quantitative determination of immunoglobulins in whole urine

Estimates of sIgA, IgG and IgM were made with the above-listed methods. The standard used was Seronorm[®] Protein (Nyegaard, Oslo, Norway). Nonconcentrated urine was used for determination of sIgA, while IgG and IgM were measured in urine after 50 × concentration. Recovery after concentration was determined in 6 samples by measuring sIgA, and was found to exceed 90 %.

Table 1. Sex, age, diagnosis and length of follow-up in patients with urinary diversion.

Method of diversion	Sex		Age (yrs)		Diagnosis	Follow-up (yrs)	
	F	M	mean	range		mean	range
Cecal reservoir	1	8	53	42-63	bladder carcinoma	3	1/2-5 1/2
Ileal reservoir	3	-	55	48-67	{ bladder carcinoma (1) interstitial cystitis (1) neurogenic bladder disorder (1)	3	1/2-5
Ileal conduit	-	3	59	54-63	bladder carcinoma	4 1/2	2-6 1/2
Colonic conduit	1	2	65	60-74	bladder carcinoma	4 1/2	3 1/2-6 1/2

Bacteria

Quantitative cultures were made from cecal reservoir urine. One strain of *E. coli* isolated from cecal urine in one patient and two strains of this species isolated from fecal samples from the same patient and from another patient were saved for hemagglutination (HA) tests. The fecal strains were selected as being among the most commonly occurring *E. coli* types (according to biochemical reactivity and antibiotic susceptibility tests).

Erythrocytes

Blood from O, Rh+ persons was collected in BD vacutainers (Becton Dickinson). Guinea pig and sheep blood was collected in 3.8% sodium citrate solution, pH 7.8. The erythrocytes were washed twice in 0.15 M NaCl. A final suspension of 1% erythrocytes in 0.15 M NaCl was prepared for use in the HA tests. Fresh suspensions were used in each test.

Hemagglutination

The three strains of *E. coli* were cultured on blood agar plates for 18 hours. The bacteria were thereafter scraped from the plates, suspended in phosphate-buffered 0.15 M NaCl (PBS), pH 7.2 and centrifuged twice at $3000 \times g$ for 15 minutes. Serial dilutions of the microorganisms were prepared in PBS. In V-shaped microtitration plates (Flow Laboratories) 25 μ l of the bacterial suspension was added to 25 μ l of the erythrocyte suspension. The plates were shaken and incubated at room temperature for one hour before read. Presence of agglutinates was determined by naked-eye inspection of the plates.

Hemagglutination tests in the presence of D-mannose

The mentioned three strains of *E. coli* were tested: 25 μ l of the bacterial suspension was mixed with 25 μ l of the erythrocyte suspension and 50 μ l of 200 mM D-mannose (Merck).

Hemagglutination-inhibition tests

From serial dilutions of the gel chromatography fraction with the highest sIgA concentration, 50 μ l was mixed with 25 μ l of a bacterial suspension containing twice the concentration of bacteria that caused visible hemagglutination. The

plates were incubated for 30 minutes at 37°C, after which 25 μ l of the erythrocyte suspension was added. The plates were kept at room temperature for 2 to 3 hours before they were read.

Results

Immunoglobulins

The gel chromatographic distribution of proteins in urine from healthy donors and from cecal reservoirs is shown in the figure. The content of high molecular weight proteins was greater in the patients than in the healthy persons.

Quantitation of immunoglobulins in the eluted fractions, using anti-IgM in single radial immunodiffusion and anti-IgG, anti-sIgA and anti-SC in electroimmunoassay, showed trace amounts of the immunoglobulins in control urine, whereas in reservoir urine sIgA in particular was abundantly present, with distribution as in the figure. As identical distribution curves were obtained with anti-sIgA and with anti-SC, IgA presumably was present predominantly as sIgA. Polyacrylamide gel electrophoresis of fractions 10–20 gave one main component with molecular weight approximately 370 000, which can be expected for sIgA. No low molecular weight substance in fractions 30–60 reacted with anti-sIgA or anti-SC, which excluded the presence of free secretory component (MW = 50 000). Small amounts of ceruloplasmin, α_1 -antitrypsin, orosomucoid and transferrin were present in fractions 20–30.

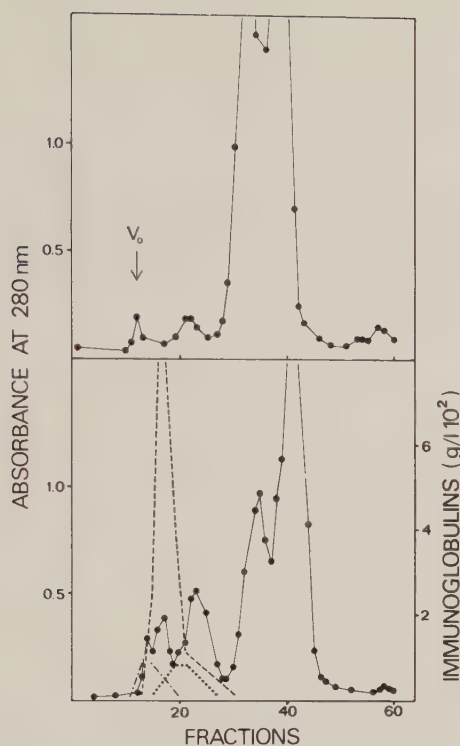
The amount of sIgA was sufficient to allow quantitation in nonconcentrated urine. This quantitation was feasible also because no other forms of IgA seemed to be present in significant amounts. IgG and IgM were determined in urine samples concentrated 50 times. The recovery of immunoglobulins from such concentrated samples was higher than 90 per cent.

The results of quantitation of urine immunoglobulins in the various groups of patients and in the controls are surveyed in Table 2. Reservoir urine contained significantly more sIgA than did conduit urine ($p < 0.001$). IgG and IgM showed no such difference. In normal urine no sIgA or IgM and only very small amounts of IgG were found. The repeated measurements of immunoglobulins in two patients with a cecal reservoir gave levels consistently within the ranges for this type of urinary diversion. No correlation between numbers of bacteria and amount of sIgA in urine was found in the cecal reservoir group.

Hemagglutination and hemagglutination-inhibition tests

The *E. coli* strains isolated from urine and from feces in one patient agglutinated human, guinea pig and sheep erythrocytes. The agglutination was mannose-resistant. The *E. coli* strain isolated from the fecal flora in another patient agglutinated erythrocytes from guinea pig and sheep, but not from humans. Also in this instance the agglutination was mannose-resistant.

The chromatographically obtained sIgA-containing fractions inhibited at a titer of 64 the hemagglutination by the urinary isolate of *E. coli*, but not that by the fecal strain from the same patient. Hemagglutination by the fecal strain from the other patient was inhibited at a titer of 8 when guinea pig erythrocytes were used and at a titer of 32 in tests with sheep erythrocytes.



Chromatography on Sephacryl S-300 of concentrated urinary proteins from intact urinary tract (above) and from continent cecal reservoir (below). Total protein (—•—•—) was measured by reading the absorbance at 280 nm. Distribution of sIgA (---), IgG (····) and IgM (—·—·—) in the effluent is indicated.

Table 2. Immunoglobulin components in urine from reservoir or conduit or from normal urinary tract.

Source of urine	sIgA		IgG		IgM	
	mg/24 h	g/mol creatinine	mg/24 h	g/mol creatinine	mg/24 h	g/mol creatinine
Caecal reservoir (n=9)						
mean	63.0	4.8	11.6	0.9	3.4	0.2
range	48.0–82.8	3.6–6.5	3.0–26.5	0.3–1.6	1.3–6.6	0.1–0.3
Ileal reservoir (n=3)						
mean	41.8	5.7	4.0	0.6	6.5	0.9
range	38–47.5	5–6.4	3–5.3	0.5–0.7	3.7–11.6	0.5–1.5
Ileal conduit (n=3)						
mean	15.6	1.3	15.7	1.3	1.6	0.1
range	4.4–25.5	0.5–1.9	4.2–28.5	0.5–1.7	0.6–3.2	0.1–0.2
Colonic conduit (n=3)						
mean	25.6	2.0	7.3	0.5	1.4	0.2
range	20.9–28.5	1.7–2.3	4.4–13.0	0.3–0.8	0.7–2.3	0.1–0.3
Normal urinary tract	none detectable		<1.8	<0.2	none detectable	

Discussion

Immunoglobulins, especially sIgA, are considered to be important in the defense of the gastrointestinal tract. Dimeric IgA is synthesized and secreted by plasma cells in the lamina propria. When diffusing through the glandular epithelial cells, IgA binds to secretory component and is released as sIgA into the intestinal lumen. Following antigen presentation, lymphocytes within the lymphoid tissue, primarily Peyer's patches, are stimulated and released to the blood via the mesenteric lymph nodes and the thoracic duct, finally homing to submucosal sites, including the lamina propria of the gastrointestinal tract, as mature plasma cells¹³.

Adherence of bacteria to epithelial surfaces is thought to be blocked by sIgA¹⁴⁻¹⁷. Intestinal bacterial colonization is inhibited also by IgG¹⁸.

IgA-producing cells are abundant in the bowel – almost 10^{10} per meter in adults. In the colon these cells constitute around 90 per cent of Ig-containing cells, whereas cells producing IgM or IgG account for 6 and 3–4 per cent¹⁹.

In the present study neither sIgA nor IgM could be detected in urine from the two controls with intact urinary tract, and IgG was present in only minute amounts. Higher concentration of urinary macromolecules from normal persons has been reported to give a 24-hour sIgA excretion of approximately 2 mg²⁰.

We found much larger amounts of immunoglobulins in diverted than in nondiverted urine, the difference being greatest for sIgA. The significantly higher content of sIgA in reservoir than in conduit urine was not accompanied by a corresponding difference in regard to IgG and IgM. It is therefore difficult to explain the reservoir-conduit sIgA difference on the basis of differences in the mucosal surface area. Nor did the use of different intestinal segments seem to explain the discrepancies. Possible explanatory factors for the variation in sIgA levels include differences in antigen stimulation due to differential patterns of infection. Further studies are required to establish if such differences do occur.

The amounts of immunoglobulins in urine from ileal conduits corresponded to earlier observations²¹. In agreement with that report, we found no correlation between the amount of sIgA and the numbers of bacteria in reservoir urine.

The mucosa of cecal urinary reservoirs has a normal appearance²², whereas mucosal atrophy is often observed in ileal conduits²³ and reservoirs²⁴. No significant differences were found in amount of immunoglobulins in urine from ileal and colonic intestinal segments, irrespective of their use as conduit or reservoir. Thus, atrophy of the ileal mucosa does not seem to influence the production of immunoglobulins.

Urinary sIgA inhibited adherence of *E. coli* isolated from reservoir urine to erythrocytes. In one patient, *E. coli* prevalent in the fecal flora, but not occurring in the cecal reservoir urine showed the same ability. This finding might support the theory of the common mucosal immune system¹³, i.e. that plasma cells primed for production of IgA antibodies home also to mucosal surfaces which are not stimulated by the antigen.

The hemagglutinating ability of *E. coli* isolated from urine was mannose-resistant, which is characteristic of P-fimbriated *E. coli*. Such strains have been stated to be pyelonephritogenic²⁵.

Our study indicates that high levels of sIgA, by preventing bacterial adherence to the mucosal surface of a cecal urinary reservoir, may constitute an important host defense mechanism there. Whether or not bacterial adherence

of the urothelium of the upper urinary tract also is inhibited by the presence of sIgA remains to be studied.

Acknowledgements

This study was supported by grants from WHO, the Maud and Birger Gustavsson Fund, Stockholm, and grants no. 16X-4709 and no. 13X-2 from the Swedish Medical Research Council. We thank Dr.L. Norlén, Gothenburg, for supplying us with urine from patients with continent ileal reservoir.

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Urine from Continent Caecal Reservoirs

Studies on chemical composition and bacterial growth

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Abstract

The composition of urine from 11 patients with continent caecal reservoir was examined with regard to promoters and inhibitors of bacterial growth, and was compared with that of urine from individuals (controls) with intact urinary tract. Reservoir urine was found to have higher and less variable pH than control urine. The concentration of urea was lower in reservoir urine, probably due to the larger 24-hour urinary output, while the concentration of albumin was higher. Although these findings could suggest reservoir urine to be a more favourable medium for bacterial growth than normal urine, such difference was not found in growth studies of common urinary pathogens. The increased prevalence of urinary tract infection in patients with caecal reservoir may be due to contamination at catheterization, residual urine and defective function of the reservoir outlet rather than differing qualities of the urine.

The past decade has seen an increased interest in methods for appliance-free suprapubic urinary diversion. A continent intraabdominal reservoir thus has been constructed in selected patients as an alternative to conduit urinary diversion. Ileum (Kock, Nilson, Nilsson, Norlén & Philipson, 1982) and caecum (Ashken, 1982; Benckroun, 1982; Månsson, Colleen & Sundin, 1984) have been utilized for reservoir construction. Intermittent clean catheterization is used to empty the reservoir, and between catheterizations the stoma is covered with a compress.

Patients with urinary reservoir usually have bacteriuria (Månsson, Colleen & Mårdh, 1984), providing a potential risk for upper urinary tract complications in the short as well as in the long run. Transmucosal shifts of crystalloids and secretion of macromolecules will result in a composition of urine differing from that in the intact bladder. Such difference may influence the conditions for bacterial colonization and growth.

The present report concerns analysis of some chemical characteristics of urine from patients with continent caecal reservoir and from persons with intact urinary tract. Bacterial growth in urine from these individuals was compared.

Material and Methods

Subjects

The study comprised 11 patients (10 male, 1 female) aged 39–63 (mean 52) years with urinary reservoir and ten controls with intact urinary tract (8 male, 2 female) aged 41–66 (mean 52) years. As part of the treatment for high-grade, invasive bladder carcinoma, urinary diversion via a continent caecal reservoir had been accomplished in the patients 6 to 66 (mean 34) months previously. Construction of the reservoir involved isolation of an ileocaecal segment and implantation of the ureters with anti-reflux technique into the caecum. Continence was ensured with an intussuscepted ileal nipple valve in the distal part of the ileum. From ileum brought through the abdominal wall, a flush stoma was fashioned (Månsson, Colleen & Sundin, 1984). The reservoir was emptied every 3 to 5 hours with clean catheterization. In the intervals the stoma was covered with a compress or a Hollister Stoma Cap® (Abbott).

Collection of urine

Urine was collected during a 24-hour period. Each portion obtained at micturition (controls) or reservoir catheterization was kept in a separate sterile glass bottle at 4°C. To prevent bacterial growth, sodium azide was added, to a concentration not exceeding 0.02M. Within four hours after the final collecting occasion, the samples were delivered to the laboratory at which time a fresh urine sample for culture and conductivity test was also supplied. The volume of each portion was determined.

Urine culture

Quantitative cultures were made on blood agar plates (Blood Agar Base, Oxoid, with 4% v/v defibrinated horse blood), using the calibrated loop technique.

Urinalyses

pH and buffering capacity. A pH-meter (pH-meter 26, Radiometer, Copenhagen) was used. Buffering capacity was determined in the pH interval 4.5–7.5 by titration with 0.1 M HCl and 0.1 M NaOH.

Free fatty acids. Head-space gas chromatography was used for tests of short-chain fatty acids. For analysis of acids with longer carbon chains (> C 8), 1 ml urine was acidified and extracted with chloroform. The free acids were then methylated, using BCl₃-methanol, and analyzed with gas chromatography (Larsson, 1983).

Standard methods were employed for analysis of **creatinine** (modified picric acid method), **urea** (urease/Berthelot method), **albumin** (electroimmunoassay using specific antihuman albumin), **glucose** (enzymatic colorimetric method), **sodium** (flame photometry), **potassium** (flame photometry), **calcium** (spectrophotometry), **magnesium** (spectrophotometry) and **zinc** (atomic absorption spectrophotometry).

Conductivity. In urine from six patients and five controls, conductivity (Conductivity meter CDM3, Radiometer, Copenhagen) and pH were determined. The bacterial numbers in the samples were determined by viable counts.

Bacterial growth studies

Strains of *Escherichia coli*, *Klebsiella pneumoniae* and *Proteus morganii* isolated from caecal reservoir urine and strains of *P. morganii* and *Proteus mirabilis* from persons with intact urinary tract were grown for 18 hours in tryptone broth (Tryptone Soya Broth, Oxoid). The bacteria were centrifuged at 2500 rpm for 10 minutes (Hettich EBA 3S) and washed three times in 0.15 M NaCl.

Urine samples from six patients and five controls were centrifuged at 3000 rpm for 15 minutes (Sorvall® RC-5B, Du Pont Instruments, Newton, USA). Aliquots of the supernatant were adjusted to pH 4.5, 5.0, 5.5, 6.0, 6.5, 7.0 and 7.5 by addition of 0.1 M HCl or 0.1 M NaOH, and then filtered through a filter with 0.2 μ m pore size (Acrodisc®, Gelman Science, Ann Arbor, USA). Samples for sterility controls were collected.

Suspensions containing approximately 10^5 bacteria/ml urine were prepared, and growth during 6 hours' incubation at 37°C was estimated by viable counts.

For viable bacterial counts serial 100-fold dilutions of urine were made in 0.15 M NaCl and 0.1 ml samples were spread on blood agar plates (as above). After incubation at 37°C for 18 hours the colonies were counted. The counts were expressed as the number of bacteria per ml.

Acid-base status

Arterial pH and base excess in the 11 patients were determined with an autoanalyzer (pH/Blood Gas Analyzer 413, Instrumentation Laboratory S.p.A., Milan, Italy)

Statistical methods

Student's t-test and Bartlett's test were used.

Results

Urine cultures

Bacteriuria was demonstrated in seven of the eleven patients with reservoir. The cultures showed *E. coli* (1 case), *K. pneumoniae* (3 cases), *Pseudomonas aeruginosa* (2 cases) and *Acinobacter* species (one case). In one control, *E. coli* was recovered. In the other subjects studied urine cultures were negative.

Chemical analyses

Concentrations of different constituents in urine from caecal reservoirs and from normal bladders are listed in Table I.

Higher **pH** values were found in urine from reservoirs than from normal bladders, with respective mean values of 6.4 and 6.1. The mean urinary pH in the four reservoir patients without significant bacteriuria was 6.1, 6.6, 6.6 and 6.7. The pH variation was less for reservoir urine than for normal urine (respective coefficients of variation 0.019 and 0.063, $p < 0.001$).

In the reservoir group, 0.24 ± 0.01 ml HCl and 0.15 ± 0.02 ml NaOH/ml urine were required to adjust the original pH to 4.5 and 7.5 respectively (mean $\pm$ SEM). The corresponding figures to express **buffering capacity** of normal urine were 0.25 ± 0.02 and 0.22 ± 0.03 . The differences were not statistically significant.

The concentrations of **creatinine** and **urea** were lower in reservoir urine than in normal urine. There was no difference in the 24-hour excretion of these constituents, however.

The concentration, and consequently the 24-hour excretion, of **albumin** was higher in reservoir urine than in control urine.

Table II presents the **conductivity** values found in urine from caecal reservoirs and from normal bladders. No significant difference in conductivity was found between the two groups. There was no correlation between conductivity and pH or number of bacteria.

Bacterial growth

Growth of *E. coli* or *K. pneumoniae* did not differ between caecal reservoir urine and control (bladder) urine at any of the tested pH levels. The numbers of bacteria after incubation for six hours at pH 5.0, 6.0 and 7.0 are shown in Fig. 1. A strain of *P.morganii* isolated from reservoir urine grew better in reservoir urine than in normal urine. No corresponding difference was demonstrable in growth of *P.morganii* or *P. mirabilis* isolated from persons with intact urinary tract (Fig. 2).

Acid-base status

The arterial pH and base excess in the patients with caecal reservoir were, respectively, 7.41 ± 0.01 and -1.3 ± 0.5 mmol/l (means $\pm$ SEM). Except in two patients with base excess -4 mmol/l, the values were within normal limits (at this hospital pH 7.35–7.45 and base express ± 3 mmol/l).

Table I. Concentration and 24-hour excretion (mean $\pm$ SEM) of some constituents of urine from urinary bladders and from caecal reservoirs.

Constituent	Unit	Urine from		<i>p</i>
		urinary bladders	caecal reservoirs	
Volume	(ml/24 h)	1160 $\pm$ 140	1830 $\pm$ 150	<0.01
pH		6.1 $\pm$ 0.1	6.4 $\pm$ 0.1	<0.05
Creatinine	(mmol/l)	11.4 $\pm$ 0.7	7.2 $\pm$ 0.4	<0.01
	(mmol/24h)	12.0 $\pm$ 0.6	13.0 $\pm$ 1.0	
Urea	(mmol/l)	312 $\pm$ 21	185 $\pm$ 15	<0.001
	(mmol/24h)	341 $\pm$ 30	333 $\pm$ 31	
Albumin	(mg/l)	<14.1	<36.1	
Glucose	(mmol/l)	2.0 $\pm$ 0.4	1.4 $\pm$ 0.2	
	(mmol/24h)	2.0 $\pm$ 0.3	2.4 $\pm$ 0.4	
Sodium	(mmol/l)	129 $\pm$ 19	96 $\pm$ 7	
	(mmol/24h)	139 $\pm$ 21	178 $\pm$ 21	
Potassium	(mmol/l)	51 $\pm$ 4	39 $\pm$ 2	<0.05
	(mmol/24h)	56 $\pm$ 5	72 $\pm$ 8	
Calcium	(mmol/l)	3.7 $\pm$ 0.5	2.3 $\pm$ 0.3	<0.05
	(mmol/24h)	4.1 $\pm$ 0.5	4.3 $\pm$ 0.8	
Magnesium	(mmol/l)	2.5 $\pm$ 0.2	1.9 $\pm$ 0.2	
	(mmol/24h)	2.8 $\pm$ 0.3	3.4 $\pm$ 0.4	
Zinc	(mmol/l)	4.3 $\pm$ 0.6	3.7 $\pm$ 0.6	
	(mmol/24h)	4.5 $\pm$ 0.5	6.4 $\pm$ 1.0	
Free fatty acids		not detected	not detected	

Table II. Conductivity, pH and number of bacteria in urine from urinary bladders and from caecal reservoirs.

Urine from	Conductivity (Siemens $\times$ cm ⁻¹)	pH	No. of bacteria/ml
Urinary bladders	0.20	5.8	<10 ³
	0.25	6.1	5 $\times$ 10 ⁵
	0.60	5.6	<10 ³
	0.60	5.5	<10 ³
	0.70	5.9	<10 ³
Caecal reservoirs	0.30	6.3	1 $\times$ 10 ⁴
	0.30	6.4	2 $\times$ 10 ⁴
	0.40	6.7	1 $\times$ 10 ⁸
	0.45	5.8	5 $\times$ 10 ⁶
	0.45	6.0	5 $\times$ 10 ⁴
	0.50	6.3	2 $\times$ 10 ⁵

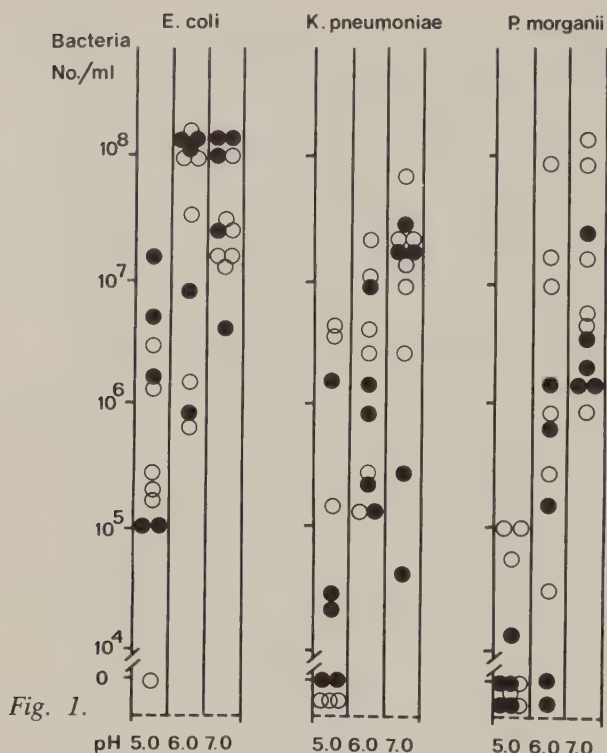


Fig. 1.

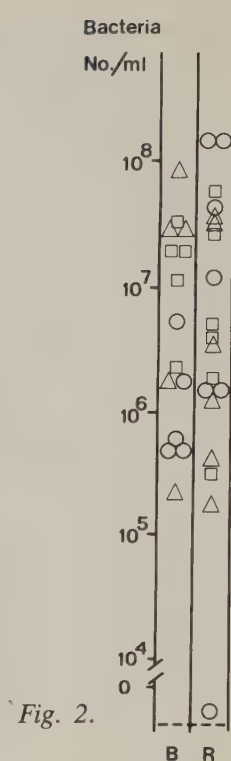


Fig. 2.

Fig. 1. Increase in number of *Escherichia coli*, *Klebsiella pneumoniae* and *Proteus morganii* after incubation for 6 hours in urine from controls (●) and from caecal reservoir patients (○) at different pH. The initial bacterial count varied between 5×10^4 and 5×10^5 bacterial/ml.

Fig. 2. Increase in number of *P. morganii* (○) isolated from caecal reservoir urine, *P. morganii* (□) and *P. mirabilis* (△) isolated from bladder urine after incubation for 6 hours in urine from intact bladders (B) and from caecal reservoirs (R) at pH 6.5. The initial bacterial count varied between 5×10^4 and 5×10^5 bacterial/ml.

Discussion

Any segment of intestine positioned in the urinary tract will cause shifts of substances across the mucosa, giving a urinary composition differing from that in the intact bladder. When urine is diverted via a continent caecal reservoir, the long time available for such transfers could be expected to imply altered conditions for bacterial growth as compared with the intact urinary tract.

In the present study, the pH of caecal reservoir urine was higher, even in the absence of infection, than in control bladder urine, and this elevated pH was constant throughout the 24-hour observation periods. The pH elevation presumably was not related to differences in tubular excretion, but more probably to changes across the reservoir wall.

Bicarbonate ions are considered to be secreted into the bowel in exchange

for chloride ions (Madsen, 1964). This tallies with the observation of slightly lowered arterial base excess in our patients with caecal reservoir. It is also consistent with previously observed slight rise in chloride and reduction in serum bicarbonate levels (Ashken). Stabilisation of the pH in reservoir urine might be attributable to the presence of albumin and certain other products released from the caecal mucosa. As the buffering capacity of reservoir urine was equal to that of normal urine, however, this mechanism seems unlikely.

The optimal pH for growth of pathogenic bacteria in the urinary tract is 6.0 to 7.0. Lower pH hampers growth (Asscher, Sussman, Waters, Davis & Chick, 1966; Kaye, 1968), one reason being the presence of organic acids (Bodel, Cotran & Kass, 1959). Weak fatty acids which provide a high fraction of undissociated molecules at the pH interval of urine are efficient inhibitors. The chromatographic studies, however, revealed no free fatty acids in reservoir urine or in normal urine. Alkaline pH of urine may also retard or inhibit bacterial growth, but only at levels not found in normal or caecal reservoir urine, i.e. at pH values exceeding 7.5 (Asscher et al.).

Because of the level and stability of pH, therefore, caecal reservoir urine should be superior to ordinary urine as a medium for bacterial growth.

At pH 6.0 to 7.0, variations of osmolality within the physiologic range of urine do not affect the bacterial growth rate (Asscher et al.). Thus, a reduced osmolality due to the increased urinary output in patients with caecal reservoir as compared to the controls with intact urinary tract was unlikely to alter the conditions for microbial growth. Conductivity provides an expression of osmolality, but we found no difference in conductivity between reservoir urine and bladder urine. Nor was conductivity related to pH or numbers of bacteria.

Certain divalent cations, e.g. Zn^{++} and Mg^{++} , can show antibacterial activity and have been proposed as important resistance factors in urinary tract infection (Youmans, Liebling & Lyman, 1938; Colleen, Mårdh & Schytz, 1975; Fair, Couch & Wehner, 1976). Such cations from the intestinal mucosa could conceivably act as defence mechanisms. However, we found no difference in the concentration of these two ions between reservoir urine and normal urine.

Urea is another urinary constituent with antibacterial effect (Schlegel, Cuelar & O'Dell, 1961; Kaye). The lower concentration of urea in caecal reservoir urine than in normal urine thus could be another risk factor promoting bacterial growth. The 24-hour excretion of urea, and of creatinine, was similar in both groups, however.

Reservoir urine contains a surplus of microbial nutrients, e.g. carbohydrates and serum proteins. The level of glucose did not differ significantly between reservoir and bladder urine in our study. However, the abundance of mucin in reservoir urine may be an important carbohydrate-containing source of energy for bacterial growth. The level of albumin was higher in reservoir urine and, in addition, such urine has also been shown to contain high levels of immunoglobulins (Månsson, Colleen, Löw, Mårdh & Lundblad, 1984).

The differences found in the chemical composition of reservoir urine and urine from intact bladders thus might be assumed to imply more optimal conditions for bacteria in the reservoirs. The growth experiments, however, did not show caecal reservoir urine to be superior as a medium for bacterial growth.

The reason for the increased prevalence of urinary tract infections in patients with a continent caecal reservoir is probably to be sought in other factors, such as bacterial contamination of the reservoir at catheterization, incomplete emptying and defective function of the reservoir outlet (Månsson, Colleen & Mårdh).

Acknowledgements

This study was supported by grants from the Swedish Medical Research Council (16X-4709) and from the Maud and Birger Gustavsson Fund, Stockholm.

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VII

The Microbial Flora of the Continent Caecal Urinary Reservoir, its Stoma and the Peristomal Skin

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Abstract

In nine patients who had undergone urinary diversion via a continent caecal reservoir, the bacteria occurring in reservoir urine, on the cutaneous stoma and on the abdominal skin were studied. In three cases, aerobic and/or facultatively anaerobic bacteria were isolated persistently from reservoir urine, while in other cases only occasionally. These organisms were isolated in pure culture. Anaerobic bacteria were also found, though infrequently, and only in conjunction with facultative anaerobes. Most stomal cultures showed heavy growth of *Staphylococcus epidermidis*, while in the abdominal skin cultures fewer microbes were isolated. *Propionibacterium acnes*, present in most skin cultures, was absent or scanty represented on the stoma. – In six patients microbial antibiosis was demonstrated in vitro between stomal and urinary reservoir bacteria. Bacteria from stomal isolates had, however, no antagonistic effect against bacteria belonging to the family of Enterobacteriaceae or against anaerobic species isolated from urine. Antibiosis may influence the microbial ecology of the urinary reservoir and cutaneous stoma.

Patients with ileal conduit urinary diversion seldom have symptoms of urinary tract infection (UTI) in the absence of obstruction. Bacteriuria nevertheless is a common finding in these patients (1,2,3). Progressive loss of renal function has been reported following ileal conduit diversion (4,5,6), with UTI and reflux attributed major causal importance (7,8,9).

Bacteria may gain entrance to the upper urinary tract by reflux from the collecting device to the conduit (10). The stoma and peristomal area are constantly soiled with urine. Hyperkeratosis and inflammatory changes are often present around the stoma, and there is heavy bacterial colonization at this site (1,2).

To obviate the problems associated with appliance-requiring urinary diversion, attempts have been made to construct a continent intraabdominal reservoir. Small series of patients diverted via a caecal (11, 12,13) or an ileal (14,15) reservoir have been reported. With such methods of diversion, the conditions for bacterial colonization may be less favourable than in a conduit. The collecting appliance of the ileal conduit is replaced by a compress only, and the skin of the peristomal area thus generally remains intact and dry.

This report concerns microbial findings in the continent caecal reservoir for urine, on the cutaneous stoma and on the abdominal skin contralateral to the stoma. In addition, antibiosis between bacteria isolated from these sites was studied in *in vitro* experiments.

Material and Methods

Patients

Nine patients (8 males, 1 female) were studied. Their age range was 42 to 63 (mean 53) years. They had undergone urinary diversion by means of continent caecal reservoir in the treatment of bladder cancer 6 to 66 (mean 38) months previously. The ureters were implanted with antireflux technique into the caecum and continence was ensured with an intussuscepted ileal nipple valve reaching the ileocaecal sphincter, which was left intact. The distal ileum was brought through the rectus muscle and a stoma was fashioned flush with the skin (11). The reservoir was emptied by clean catheterization at intervals of three to five hours. At all other times the stoma was covered with a compress or Hollister Stoma Cap® (Abbott). In two patients there was risk of leakage at high filling of the reservoir. Three of the patients received trimethoprim 100 mg daily as prophylaxis against UTI.

Sampling techniques and isolation procedures

Sampling and culture procedures for studies of the microbial findings were performed once monthly for three or four months. The microbes used in the antibiosis tests were isolated at a later occasion.

Urine. Samples obtained by routine clean catheterization of the reservoir were cultured for aerobic, facultatively anaerobic and strictly anaerobic bacteria, mycoplasmas, ureaplasmas and yeast fungi.

Urine for bacterial cultures was transferred immediately after sampling into tubes containing 90% CO₂ and 10% H₂ and was processed in the laboratory within two hours. Quantitative cultures were made on blood agar plates (Blood Agar Base, Oxoid, with 4% v/v defibrinated horse blood), using the calibrated loop technique. The plates were read after overnight incubation at 37°C.

Blood agar plates supplemented with either 5 µg hemin (Sigma) and 0.5 µg vitamin K₁ (Merck) or with 100 µg kanamycin (Ferrosan) per ml were also used. The plates were incubated at 36–37°C for 48 hours in a Whitley Anaerobic Cabinet (Assab, Solna, Sweden) in an atmosphere of 10% CO₂, 10% H₂ and 80% NO₂.

For isolation of *Mycoplasma hominis*, Heart Infusion Agar (Difco) and for *Ureaplasma urealyticum*, a modified Shepard's medium, was used (16). The plates were incubated in 10% CO₂ atmosphere for three to five days before they were read under a stereomicroscope. For isolation of yeast fungi, Sabouraud Dextrose Agar (Oxoid) was used. Two plates were inoculated and incubated at 30°C and 37°C respectively, for five days before they were read.

Stoma/peristoma and contralateral hypochondrium. Contact agar plates (Ø 6 cm, surface area 28 cm², Nunc, Denmark) consisting of blood agar (see above), were used. On each sampling occasion one plate was pressed against the stoma and another against the skin of the contralateral hypochondrium for a few

seconds. The plates were incubated for 48 hours in a Whitley Anaerobic Cabinet before they were read.

Antibiosis test of bacteria from different sampling sites. Bacteria isolated from stoma and contralateral hypochondrium in nine patients were tested for growth-inhibiting capacity against bacterial isolates from urine, and vice versa, essentially according to a previously described technique (17). Overnight cultures were used. A few colonies of bacteria isolated from stoma/peristoma or contralateral hypochondrium and from urine were cross-inoculated on a solid growth medium (20g Nutrient Agar (Oxoid), 5g Tween 80, 5 g glucose and distilled water ad 1000 ml, pH 6.5). The plates were incubated overnight at 37°C. Antibiosis was defined as a distinct zone of growth-inhibition (showing no or only single colonies) that could be observed with the naked eye.

Results

Urine cultures

Bacteria were isolated from the urine of six of the nine patients (Table 1). Three patients showed on all sampling occasions growth of facultatively anaerobic bacteria, viz. *Klebsiella pneumoniae*, *Escherichia coli* or *Pseudomonas aeruginosa*. In two of these patients there was risk of urinary leakage at high filling of the reservoir. Three other patients had intermittent bacteriuria. Sterile urine was found at all occasions in three patients, two of whom received trimethoprim therapy. A mixed flora of these organisms was found in only 2 of the 34 tested samples.

Strictly anaerobic bacteria, as a rule several species concomitantly, were in three cases isolated intermittently, and always in conjunction with facultatively anaerobic species. Various species of *Fusobacterium*, *Bacteroides*, *Veillonella*, *Peptococcus* and *Peptostreptococcus*, were recovered.

Mycoplasma hominis was never found, while *Ureaplasma urealyticum* was recovered once. Interpretation of the cultures for mycoplasmas, however, was rendered impossible by overgrowth of bacteria in 11 of 34 samples.

Yeast fungi were in no case isolated.

Stoma/peristoma and contralateral hypochondrium cultures

The organisms most commonly isolated from the stomal area and the skin of the contralateral hypochondrium are listed in Table 2. Patients with bacteriuria generally were more heavily colonized at stoma level. *Staphylococcus epidermidis* was the most common isolate both on the stoma and on the skin, though it occurred in lower numbers on the latter site. Various species of *Bacteroides* and *Peptococcus* were isolated more frequently from stoma than from skin. *Propionibacterium acnes* on the other hand, was seldom isolated from the stomal samples. When species of *Bacteroides* were recovered from reservoir urine, they were always present on the stoma, while the reverse was not necessarily true. *Peptococcus magnus* could be isolated from the stoma in all patients, but rarely from urine specimens.

Table 1. Quantitative urine cultures for aerobic, facultatively and strictly anaerobic bacteria and mycoplasmas in patients with continent caecal urinary reservoir. (In cases 1*, 3* and 5 no growth was found).

Microorganism	Case 2*, month 2 3 4				Case 4, month 3 4				Case 6, month 1 2 3 4				Case 7, month 1 2 4				Case 8, month 1 2 3 4				Case 9, month 1 2 3 4			
Gram-negative rods, unclassified	S	S											S											
<i>Acinetobacter</i> species	H	M																						
<i>Klebsiella pneumoniae</i>					H	H			H	H	H		H	S										
<i>Proteus morganii</i>					H																			
<i>Escherichia coli</i>																	H	H	H					
<i>Pseudomonas aeruginosa</i>																								
Anaerobes					H								M	H			H	H						
(see text)																								
<i>Ureaplasma urealyticum</i>																								

Abb.: S = sparse growth (<10⁴ CFU/ml), M = moderate growth (10⁴–10⁵ CFU/ml), H = heavy growth (> 10⁵ CFU/ml).
 * Prophylactic treatment with trimethoprim (100 mg daily) had been given
 ** Organisms recovered, but quantitative culture not performed.

Table 2. Microbial flora of stoma (numerator) and contralateral hypochondrium (denominator) in patients with continent caecal urinary reservoir (total no of colony-forming units/28 cm² contact agar plate) at 3 (case 1 and 3) or 4 sampling occasions. * Prophylactic treatment with trimethoprim (100 mg daily) given.

Microorganism	Case 1*, month				Case 2*, month				Case 3*, month				Case 4, month				Case 5, month			
	1	2	3		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
<i>Acinetobacter</i> sp.		6	3			200			150	200			150	100	100	200				
			8			50							25	50	15	50				
<i>Staphylococcus epidermidis</i>	50	5	2		150	200	150	200	500	200	150		75	100	50	35	300	300	400	150
	25	10			10	25	10	10	70		5						50	200	100	25
<i>Bacteroides melaninogenicus</i>					100	100	200						100	200	25	50	200	200	200	15
<i>Bacteroides ureolyticus</i>													200	200	50	50				10
							50	50					50			3				100
<i>Peptococcus magnus</i>	10				250	150	150	100	75	100	25		150	150	15	25	200	175	100	
										10			25	75		15	150	75	5	
<i>Propionibacterium acnes</i>	5				10	3	15	5		5			45		25	25	200	200	25	15
	2	2																		

Microorganism	Case 6, month				Case 7, month				Case 8, month				Case 9, month			
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
<i>Acinetobacter</i> sp.		400	100						200	100	200	400	150	400	400	100
		160							100		10	5	15	5	20	25
<i>Staphylococcus epidermidis</i>	25	200	5	10	200		200	100	150	300	200	500	200	200	250	200
					100	175	75	50	200	40	25	15	80	15	30	50
<i>Bacteroides melaninogenicus</i>				5	500	200	400		200	500	500	500	500	400	500	300
<i>Bacteroides ureolyticus</i>		100								200	200	300				
									10							
<i>Peptococcus magnus</i>	150	400	400	25	450	250	400	100	75		250	200	200			100
		50	5	5		280		40	150						25	50
<i>Propionibacterium acnes</i>						50		25	100							
		5	10	10					5		5	10				

Table 3. In vitro interaction between bacteria isolated from urine, and from stoma/contralateral hypochondrium in 6 patients with continent caecal reservoir.

Patient	Isolate(s) from urine	Growth of urinary organisms inhibited by from stoma	Urinary organisms inhibited by from hypochondrium	Urinary organisms inhibited growth of from hypochondrium
2	Micrococci			
	Gram-positive rods (nonidentified)	<i>P. aeruginosa</i>	<i>S. epidermidis</i>	
3	<i>Acinetobacter</i> species (strain I)	<i>S. epidermidis</i>	<i>S. epidermidis</i>	
	<i>Acinetobacter</i> species (strain II)	<i>S. epidermidis</i>		
	<i>Alkaligenes</i> species	<i>S. epidermidis</i>		
	<i>Staphylococcus aureus</i>		<i>S. epidermidis</i>	
4	<i>Acinetobacter</i> species	<i>Alkaligenes</i> sp. <i>Acinetobacter</i> sp. <i>P. aeruginosa</i>	<i>Acinetobacter</i> sp.	
5	<i>Staphylococcus epidermidis</i> α -streptococci (strain I) α -streptococci (strain II)	<i>E. coli</i> <i>E. coli</i> <i>E. coli</i>	<i>Ent. aerogenes</i> <i>Ent. aerogenes</i> <i>Ent. aerogenes</i>	
7	α -streptococci			<i>S. epidermidis</i> <i>Bacillus</i> sp.
9	<i>Pseudomonas aeruginosa</i>			<i>K. pneumoniae</i> <i>S. epidermidis</i> <i>P. aeruginosa</i> <i>P. aeruginosa</i>

Antibiosis tests

No antibiosis was demonstrable in three of the nine cases studied. It seemed noteworthy that these were the only patients in whose reservoir urine bacteria belonging to the family of Enterobacteriaceae (*Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*), were found. Nor was any inhibition observed when strains of *Bacteroides fragilis* and *Clostridium perfringens* from three patients' urine were tested.

Antibiosis could be demonstrated in six patients between certain intermittently occurring urinary isolates and isolates from the own stoma and/or contralateral hypochondrium. Nevertheless, such microbes isolated from urine were not seldom present at the stoma as well (Table 3).

Discussion

Urinary tract infections are common in patients with urinary diversion and have been considered to cause progressive impairment of renal function. When no obstruction is present, such impairment has been ascribed to reflux of infected urine (7,8,9).

Culture studies have indicated that a urostomy appliance attached to the peristomal area creates a moist chamber between the skin and the appliance, and thereby favourable conditions for bacterial growth. The stoma and the distal part of the ileal conduit in patients wearing a urostomy appliance usually are heavily colonized with bacteria, as a rule a mixed flora of coliforms, *Proteus* and *Pseudomonas* species and bacteria normally present on the skin (2). When a double-lumen catheter was used for sampling, thus avoiding contamination from the stoma and distal part of the conduit, urine collected at the proximal end of the conduit yielded growth less often or of sparser type than in urine collected at the stoma (1,2). Residual urine in the conduit (8) and reflux from the appliance bag (10) seem to favour bacterial colonization of the conduit. Considerable variation in species and number of organism recovered from ileal conduits has been reported (18). Such infections did not respond to antibiotic treatment (18,19).

When urinary diversion is accomplished via a continent reservoir, a "dry" stoma can be achieved. This stoma needs only a compress for cover. By clean intermittent catheterization the reservoir is emptied at intervals of three to five hours. With such surgical technique and emptying procedure the peristomal skin remains intact and there are few problems of local infection. Favourable functional results have been reported from use of caecum (11,12,13) and ileum (14,15) as reservoir.

In our study, bacteria were recovered from 20 of 34 samples of caecal reservoir urine. In three patients the urine contained aerobic or facultatively anaerobic bacteria on all sampling occasions. Two of these patients faced the risk of leakage at high filling of the reservoir. Other authors have reported persistent or intermittently occurring bacteriuria in most patients with caecum (11,12) or ileum (14,15) as urinary reservoir. Bacteriuria is common also when the lower urinary tract is intact and clean intermittent catheterization is done for conditions such as neurogenic bladder disorder (20, 21). When aerobic, i.e. *Pseudomonas aeruginosa*, or facultatively anaerobic bacteria were found in caecal reservoir urine, the infection almost always was caused by a single bacterial species. This agrees with findings in colonic conduits (3), whereas in ileal conduits a mixed flora generally was found (3). Urine from colonic conduits was more often sterile than urine from ileal conduits (3). The differ-

ence tallies with an earlier report that bacteriuria was seldom found after colonic conduit urinary diversion (22).

The appearance of the colonic mucosa remains normal even after several years of contact with urine (11, 23), but in the ileal conduit and reservoir villous atrophy is often seen (24, 25). No correlation between the bacterial flora and the extent of histologic mucosal changes in ileal conduits has been reported, however (26).

From caecal reservoir urine we found that obligate anaerobes could only be isolated concomitantly with facultative anaerobes. This generally applies also in the few instances in which such bacteria occur in the intact urinary tract. In the intact colon obligately anaerobic organisms greatly outnumber aerobes and facultative anaerobes – by 1 000 to 10 000:1 (27).

Our study of the microbial flora of the stoma/peristoma and the skin of patients with caecal reservoir suggested that the flora at these sites remains fairly stable. Various species of *Bacteroides* were almost always present on the stoma, but were seldom recovered from urine.

From urine collected by clean intermittent bladder catheterization, streptococci and *Staphylococcus aureus* can sometimes be recovered (21), which suggests contamination from the skin flora. Such a mechanism may be present also in patients with caecal reservoir. In persons with intact urinary tract, the perineal hygiene seems to be of little importance in the aetiology of UTI (28, 29). In UTI-susceptible persons, the infection is often preceded by abnormal periurethral colonization (30, 31). In patients with caecal urinary reservoir, the occurrence of bacteriuria and the quantity of bacteria at stomal level seemed to correlate. This corresponds to the concept of the "infectious dose", i.e. that the number of bacteria colonizing the mucosal surfaces in the distal part of the urinary tract is important for the establishment of UTI.

The elimination of microorganisms conveyed into the reservoir may be facilitated by local production of immunoglobulins preventing bacterial adherence to the mucosa. In caecal urinary reservoir the level of secretory IgA is high (32). Secreted mucin, which likewise is abundantly produced, might act as receptor analogues and trap bacteria (33).

Another mechanism reducing the risk of colonization and consequent infection may be antibiosis. In our in vitro experiments, however, no such interactions were found between, on the one hand, established common urinary pathogens of the family of Enterobacteriaceae and, on the other hand, stomal or skin bacterial isolates. This might be one contributing factor why these urinary pathogens could be recovered from the reservoir in some patients. Antibiosis was however found in cases when growth of species occasionally recovered from urine, but not regarded as primary pathogens, e.g. species of *Acinetobacter*, *Alkaligenes* and various types of staphylococci, micrococci and streptococci were inhibited by stomal or skin bacteria. Though these urinary microbes often occurred on the stoma as well, it is worthy of consideration that the intussuscepted nipple valve, in addition to its function of high-pressure zone preventing escape of urine, might act as an ecologic barrier against bacterial colonization of the reservoir. Better condition for bacterial colonization of the reservoir thus might be present if the nipple valve is unreliable; i.e. closes imperfectly with risk of urinary leakage. This was the case in two of our patients.

UTI in patients with urinary diversion via a continent caecal reservoir seems to have a benign course. Renal function is well preserved (34). Eighteen patients with such reservoir have hitherto been followed up by us for a total of 740 months. Only one patient has had symptoms of UTI. This patient, who had stricture of one of the ureterointestinal anastomoses and developed

pyelonephritis, illustrates the danger of UTI in conjunction with obstruction in the urinary tract, rather than the risk entailed by bacteriuria per se.

Acknowledgements

This study was supported by grants from the Swedish Medical Research Council (16X-4709) and from the Maud and Birger Gustavsson Fund, Stockholm.

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